FEB - 1 1935

Pharmacy, as a Profession, Will Always Go Forward. The Professional Pharmacy of To-day Is the Pharmacy of Yesterday, Succeeding the Old Apothecary Shop. It Has Kept Up with the Pace of Progress and Is Continuously Progressing toward the Highest Type of Professional Service.

Vol. XXIV, No. 1 JANUARY, 1935

JOURNAL

OF THE

AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

CONTENTS

Frontispiece and Sketch—Dr. Fred B. Kilmer 3
Editorial:
The New Year 4
Signs of Progress in Pharmacy 4
A New U. S. P. X Interim Revision of the Ergot Assay—Cook 5
Scientific Section:
Continuous-Reading Titration Apparatus—Baldinger 6
A Note on the Assay of Reduced Iron—Oakley and Krantz, Jr. 9
Assay Methods for Salts of Organic Acids—Hitchens 11
Digitalis Assay on Normal and Exsanguinated Cats—Macht 15
Methods of Identification of the Rhizomes of Iris Versicolor L. and Iris Virginica L.—Hocking 17
A Study of a New Series of Urethanes—Lott and Christiansen 22
The Active Constituents of Ergot: A Pharmacological and Chemical Study—Thompson 24
Antidotes. I. General Plan—Munch and Garlough 38
Bibliography of Pharmaceutical Research—DuMez 40
The Stabilization of Syrup of Hydriodic Acid, U. S. P. X—Husa and Klotz 45
A Study of Vehicles for Medicines—Fantus, Dyniewicz and Dyniewicz 46
Hospital Pharmacy Practice: An Innovation—Mordell 50
History in the Drug Store—Kilmer 55
History of the Calcium Lactophosphate Preparations—Husa and McLean 58
The Department of the American Association of Colleges of Pharmacy:
Food and Drug Legislation—Little 61
Association Business 64
Testimonial Dinner to R. P. Fischelis, President of the American Pharmaceutical Association, Hotel Pennsylvania 69
Proceedings of the Local Branches 70
F. E. R. A. Prescription Price Schedule—Seltzer 76
Editorial Notes 78
Personal and News Items 79
Societies and Colleges 80
Legal and Legislative 82
Obituary 86
Book Notices and Reviews 88
Notice to Contributors to the Journal American Pharmaceutical Association 90
Advertising—Cover Pages 2, 3 and 4 and pp. I–XXII.

Published Monthly by the American Pharmaceutical Association: Office of Publication, 20th & Northampton Sts., Easton, Pa. Editorial Office, 2215 Constitution Ave., Washington, D. C. Annual Subscription, $4.00; Canada, $4.35; Other Foreign, $4.50; Single Numbers, 35 cents; Canada, 40 cents; Other Foreign, 50 cents.

THE 83rd ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN PORTLAND, ORE., IN 1935.

Local Secretary, A. O. Mickelsen, School of Pharmacy, Portland, Ore.

The 1935 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Portland.

Entered as second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103 Act of October 3, 1917; authorized July 10, 1918.

THE ADMINISTRATION BUILDING OF THE PUBLIC HEALTH SERVICE.*

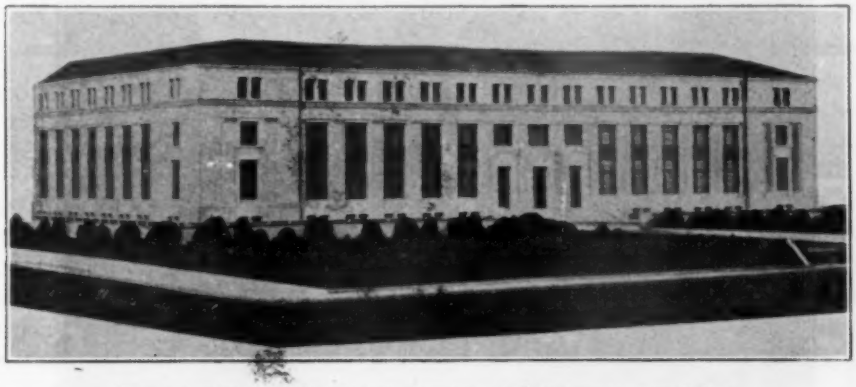
"The United States Public Health Service dates almost from the very beginning of our national history. It had its origin in a law enacted by the Federal Congress in 1798, which established the marine hospitals to provide relief and maintenance for sick and disabled American seamen. This was an important step in furthering the development of a great merchant fleet and the expansion of American commerce. Some of these hospitals cared for officers, sailors and prisoners wounded in naval engagements of the War of 1812."

The following is a very brief, general outline of the activities of the Public Health Service in fulfilling its important duties and responsibilities in protecting the health of the people:

Control of maritime quarantine, examination of immigrants, and inspection of passengers and crews of vessels and airplanes arriving from foreign ports, to protect the country from the importation of dangerous communicable diseases.

Control of interstate quarantine and health matters involved in interstate traffic, to prevent the spread of communicable diseases between the States.

Study of the cause and means of propagation and spread of diseases of mankind, and the development of methods of prevention and control. In this work the Public Health Service maintains



Bureau of the Public Health Service—Administration Building.

several research laboratories, the most important of which is the widely known National Institute of Health in Washington, D. C.

Supervisory control and licensing of the manufacture of biological and analogous products used in the prevention and treatment of diseases, to insure safe and standard products. These include the various vaccines, serums, antitoxins, arsenicals and similar preparations.

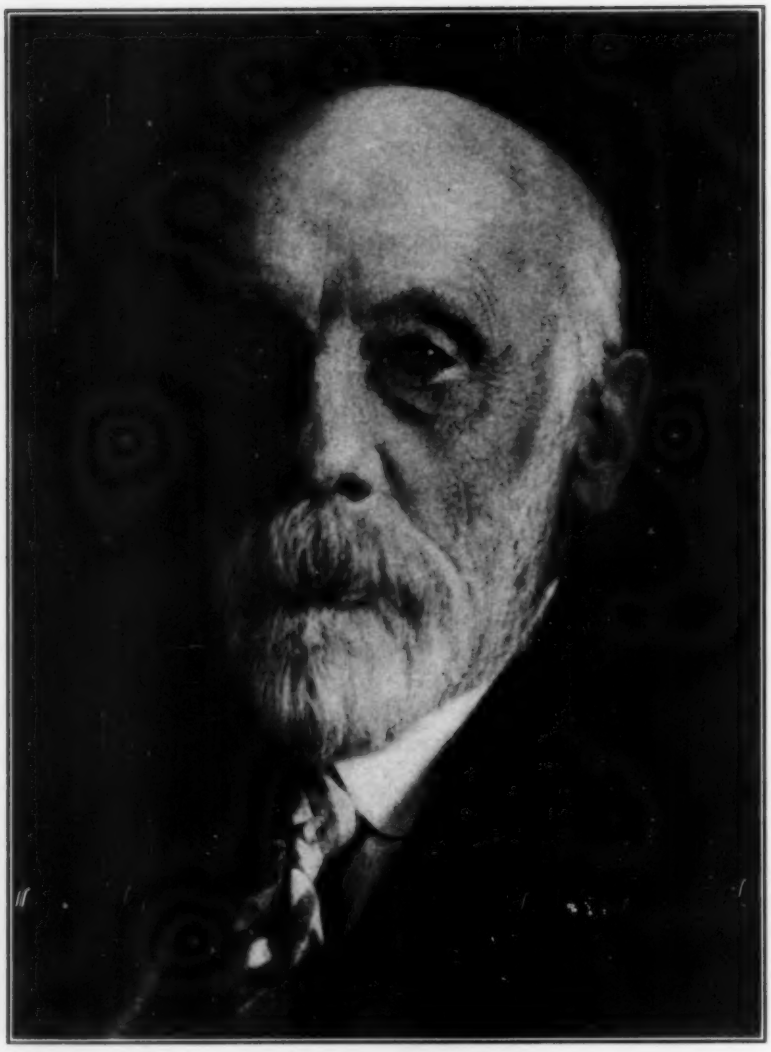
Study of mental diseases and drug addiction and the investigation of legitimate needs for narcotics.

Coöperation with State and local health departments, upon request, in all matters pertaining to public health.

Collection and publication of reports of disease prevalence in the United States and foreign countries, and compilation and publication of State laws and regulations and of court decisions relating to public health. Public health education and the dissemination of public health information.

"The affairs of the Public Health Service are administered by the Surgeon General and assistant surgeons general in charge of administrative divisions located in the Administration Building in Washington, D. C. On July 1, 1933, the personnel consisted of a total of 4911 persons. These include physicians, dentists, pharmacists, nurses, dietitians, laboratory technicians and other employees—a small army of trained personnel whose work is protecting the health and lives of the people of the United States. The career officers of the Public Health Service are commissioned by the President, and they constitute a mobile sanitary corps whose members are available for service anywhere in the United States or foreign countries. Such a mobile corps is indispensable for the control of epidemics, quarantine duty and the prosecution of investigative studies."

* Third building east of the American Institute of Pharmacy on Constitution Ave., Washington, D. C.



DR. FRED B. KILMER.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXIV JANUARY, 1935 No. 1

F. B. KILMER WILL SETS UP PRIZES FOR PHARMACY.

The will of Frederick Barnett Kilmer, filed for probate January 12th, includes bequests to the American and New Jersey Pharmaceutical Associations for prizes for meritorious work. Provision for the prize to be awarded by the AMERICAN PHARMACEUTICAL ASSOCIATION was made in a $3000 trust fund, the income of which is to be applied by the ASSOCIATION to the rewarding of meritorious work in pharmacognosy. A fund of $1000 was set aside for the New Jersey Pharmaceutical Association, the income to be awarded annually to the author of the best paper submitted to the association by a graduate pharmacist.

Mr. Kilmer also left a $5000 fund to St. Peter's General Hospital, in New Brunswick, to perpetuate the nurses' library founded there in honor of Joyce Kilmer. Christ Episcopal Church in New Brunswick will receive $1000 to be applied with other funds to the erection of a memorial to the Rev. E. B. Joyce, former rector of the Church, and the income from a $2000 fund for the preservation of historical data connected with Christ Church. Books and manuscripts in Mr. Kilmer's library, which were written by his son, were left to Rutgers University, and other books, mostly scientific in nature, were left to the Philadelphia College of Pharmacy and Science, to St. Peter's General Hospital, New Brunswick, and to the residuary legatees, all of whom are members of the family.

EDITOR'S NOTE: Mr. Kilmer became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1886. He was deeply interested in the Section on Historical Pharmacy, and in recent years the articles he contributed to the ASSOCIATION dealt with historical subjects.

Mrs. Kilmer died December 31, 1931; a brief sketch may be found in the January JOURNAL, 1932, page 93, and a notice of Dr. Kilmer's death appears in this issue of the JOURNAL.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

THE NEW YEAR.

LIFE is kaleidoscopic, it is ever changing—that is true under all conditions and situations and more so when affairs have been shaped so that some radical changes and directions seem necessary. The call is for master minds, seriously directed, not only to correct but watchful that the direction may be toward a betterment of a greater number. One of the evidences of life is that man is not ready to apply the Golden Rule in civic, social, financial, commercial and industrial problems; he seems to prefer business depressions and fosters social and ethical complexities. There is a willingness on the part of some to have others follow the right course or remain inactive and quiet until there is ponderous evidence of misdirection or until their own activities are affected. This is true not only in financial and commercial affairs, but in professional life; thereby the public suffers. We cannot hope for perfection, nor can we expect that there will be decided improvement unless fear and selfishness which retard progress will be overcome to a greater extent and make it possible to adjust matters.

We invariably enter a new year with hopes as well as uncertainties, realizing that efforts rightfully applied will make for progress, but that disappointments will be encountered. It is necessary that we have confidence in our fellow men and co-workers and it is with the determination to do our part that we venture upon new experiences. The best way to do business and advance professional service is to join with others in well-directed efforts.

SIGNS OF PROGRESS IN PHARMACY.

ASIDE from the papers of the Scientific Section, every other division of the program of the AMERICAN PHARMACEUTICAL ASSOCIATION has shown a purpose to improve the practice of pharmacy. Reference is made to the researches relative to drug extraction, how and why there is variation in dosage of prescriptions. It has emphasized that the individual needs not only experience but a knowledge which enables him to understand what he sees and does. Series of articles dealing with the subjects have appeared in the JOURNAL and will, no doubt, stimulate the studies and result in a better understanding and realization of the importance of prescription practice, which in turn enables physicians to comprehend why the results of their prescribing may lack the uniformity which they expect, and gives them greater assurance that by closer coöperation, studies and conferences their practice will be improved; thereby better service is rendered the public. It should impress the fact that medicine, including dentistry and pharmacy, has other problems which concern members of these professions and it is gratifying to note that this spirit of coöperation is being strengthened.

There are promotions which apply especially to pharmacy in which the other divisions of medicine should take an active part and pharmacists should be helpful

in activities that enable the related professions to improve their service. Reference is here made to legislation, regulation of practice, revision of the standards, and changes that may come about through plans of President Roosevelt's Committee on Economic Security. In all of these the professions have an interest and to make them more effective and serve their purposes mutual studies by the professions are essential and helpful factors.

A NEW U. S. P. X INTERIM REVISION OF THE ERGOT ASSAY.

E. FULLERTON COOK, CHAIRMAN, U. S. P. COMMITTEE OF REVISION.

THE first interim Revision of the Tenth Revision of the Pharmacopœia became official on January 1, 1934, and made certain changes in the assay of ergot and its fluidextract, also a modification of the manufacturing method for the fluidextract of ergot. In the first revision, the standard for ergot remained as in the original text, namely, a fluid preparation of ergot.

Since then, however, as a result of further investigation, it has been found desirable to adopt the alkaloidal salt, ergotoxine ethanesulfonate, as the official ergot standard.

For the purpose of insuring uniformity in the ergotoxine ethanesulfonate to be used as the official ergot standard, the U. S. P. Board of Trustees has arranged for the packaging in ampuls, under nitrogen, of a carefully standardized lot of this alkaloidal salt. This ergot standard may be obtained through the office of the Chairman of the U. S. P. Committee of Revision, 43rd Street and Woodland Avenue, Philadelphia, Pa.

By this new revision (No. 3) ergot will be required to possess a potency, per gram, equivalent to not less than that of 0.5 mg. of the official standard and the fluidextract must be adjusted to possess a potency, per cubic centimeter, equivalent to that of not less than 0.4 mg. and not more than 0.65 mg. of the standard ergotoxine ethanesulfonate.

The new monographs for ergot and fluidextract of ergot released in Interim Revision No. 3 on January 1, 1935, will become official and enforceable on May 1, 1935. Anyone desiring a copy of the "Interim Revision Announcement No. 3" may obtain it by addressing the Chairman, E. Fullerton Cook, 43rd Street and Woodland Avenue, Philadelphia, accompanying their request with *ten cents in stamps* to cover printing and distribution.

TERCENTENARY OF CHEMICAL INDUSTRIES.

The year 1935 will mark the three hundredth anniversary of the establishment of the chemical industries in America. This anniversary will be celebrated by the American Chemical Society at its annual spring meeting during the last week of April of that year. Elaborate plans of the Society's New York Section, now well under way, indicate that this celebration will be a memorable one in the annals of American industry. Leaders in industry, finance and government will unite with the 17,000 members of the American Chemical Society to celebrate three hundred years of achievement of the American chemical industries.—*Industrial and Engineering Chemistry.*

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins, George D. Beal, L. W. Rising, H. M. Burlage, L. W. Rowe, John C. Krantz, Jr., Heber W. Youngken.

CONTINUOUS-READING TITRATION APPARATUS.*

BY LAWRENCE H. BALDINGER.[1]

As an aid in presenting the subject of electrometric titration to a class in Analytical Pharmacy, a simple, inexpensive apparatus was constructed which was rugged enough to withstand frequent use by students, sufficiently accurate to emphasize continuous-reading electrometric titration methods. The apparatus as described can be assembled and wired in about three hours. All of the parts of the apparatus except the galvanometer and the milliammeter can be purchased from a radio dealer. The total cost should not exceed twenty-five dollars.

Discussion.—The ordinary potentiometric titrations involve the reading and plotting of E. M. F. values of the titration cell *versus* the milliliters of reagent used. Using the vacuum-tube apparatus no plotting is necessary unless desired for laboratory records. Instead of using a "balanced" circuit, *i. e.*, a circuit in which the E. M. F. of the titration cell is balanced against a known E. M. F., the vacuum-tube apparatus employs an "unbalanced" circuit in which the course of the reaction is followed by observing galvanometer deflections. The theory upon which this apparatus is based, as well as a description of the newer wiring diagrams and uses, has been discussed in the literature (1). Inasmuch as some difficulty was experienced in duplicating results using some previously reported wiring diagrams, the apparatus used in this work was finally assembled according to the method of Goode (*loc. cit.*). See Fig. 1.

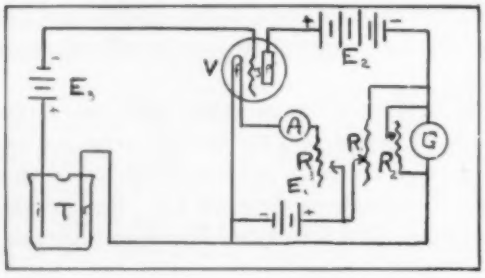


Fig. 1.—Continuous-reading titration apparatus.—V, electron tube; f, filament; p, plate; g, grid; T, titration cell; i, platinum indicator electrode; r, reference electrode; G, galvanometer; A, milliammeter; R_1, 25,000 ohm rheostat; R_2, 25 ohm rheostat; R_3, 85 ohm rheostat; E_1, 3-volt battery; E_2, 22.5-volt battery; E_3, 1.5–4.5-volt battery.

In addition to the ease with which the course of a reaction can be followed by observing the galvanometer deflections, this type of apparatus offers the advantage over the potentiometric method of titration in that the vacuum tube operates as a voltmeter which draws practically no current from the titration cell.

The heated filament (f) emits a stream of electrons which impinge upon the plate (p) setting up a current which activates the galvanometer (G). The current in the galvanometer circuit is made up of two parts: (*a*) the residual plate current, and (*b*) that current which is a function of the grid bias developed by the electrodes of the titration cell. As the grid bias is changed the plate current is altered correspondingly depending upon the amplification factor of the vacuum tube The residual plate current is so large in comparison with the current which is a function of the

* Scientific Section, A. PH. A.

[1] Instructor in Pharmacy, University of Notre Dame, Notre Dame, Indiana.

grid bias that it must be balanced by an equal and opposite current before a titration can be performed. An *RCA Radiotron* tube, type *UX-199*, drawing 0.04–0.05 ampere current at optimum operation, was used in this apparatus. A plate voltage of 22.5 volts was found to be sufficient for our work. Although additional grid bias was not needed in our experiments, C-battery terminals were provided on the panel. A 25-ohm variable resistance (R_2) acts as a galvanometer shunt. The current of the filament battery acting through a 25000-ohm variable resistance (R_1) serves to balance out the residual plate current and thereby to increase the sensitivity of the galvanometer. The *D'Arsonval* galvanometer[1] (G) is an inexpensive model having a resistance of 150 ohms and a sensitivity of 1.7 megohms at 12.5 cm. The milliammeter (A) may be either a portable or panel type. See Figs. 1 and 2.

In order to simplify still further the apparatus used, graphite and platinum, tungsten and platinum, and silicon carbide-platinum electrode pairs were used in place of the calomel half-cell-platinum assembly as proposed by previous workers. Inasmuch as only E. M. F. changes, not actual values, are observed with this apparatus, nothing is to be gained by the use of the calomel half-cell, provided that other electrodes will give consistent results. Brünnich (2) has employed the graphite and platinum electrode pair in neutralization reactions, connecting the electrodes directly to a galvanometer through a tapping key. Depolarization of the electrodes, an obvious result of prolonged key contact in Brünnich's assembly, is eliminated by the use of the vacuum-tube voltmeter. Furman and Wilson (3) have extended the use of the tungsten-platinum electrodes to oxidation-reduction titrations in a system analogous to that of Brünnich. Kamienski (4) showed that silicon carbide is an ideal substance to use as a constant reference electrode since its potential is almost independent of the chemical properties of the solution in which it may be immersed. The electrode systems were constructed in compact units in order to minimize breakage. See Figs. 2 and 3.

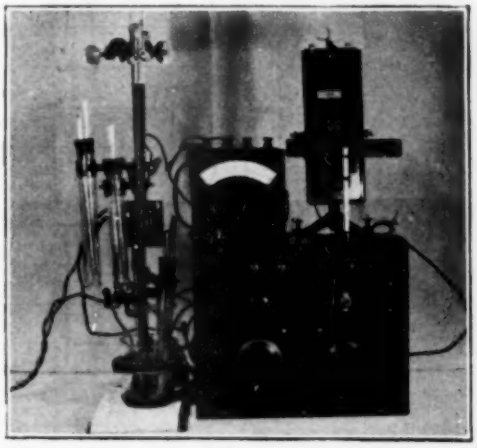


Fig. 2.—Titration apparatus.

For the titration of strong acid with strong base, weak acid with strong base, and iodine with sodium thiosulphate, it was found that the graphite and platinum electrode pair gave satisfactory results. Both the tungsten-platinum assembly and the silicon carbide-platinum electrodes gave good results in the titration of ferrous ammonium sulphate with potassium dichromate solution. In all experiments the electrometric titrations were checked using standard methods of analysis. The galvanometer deflections were plotted *versus* milliliters of reagent and curves were drawn through the points to show the course of the reaction. See Fig. 4. In order to show the practicability of this apparatus in a course in Analytical Pharmacy, a number of ferrous iron preparations of the U.S.P. were analyzed, using the tungsten-platinum and the silicon carbide-platinum assemblies. Simultaneously with the use of the vacuum-tube apparatus, the titrations were checked, using diphenylamine

[1] Central Scientific Co., Chicago, Ill. Catalog No. F-4451.

as an indicator. In practically all of the titrations of these compounds, it was found that about 0.15 ml. more of potassium dichromate solution was necessary to reach a diphenylamine end-point after the end-point had been indicated by the apparatus. This is in agreement with the findings of Knop (5) and of Kolthoff and Sarver (6) who have suggested a correction factor for the oxidation of diphenylamine.

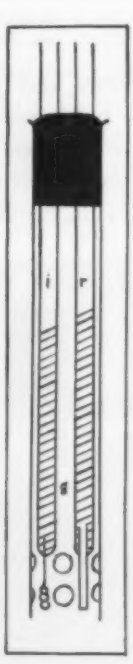


Fig. 3.—Electrode assembly: i, platinum electrode; r, reference electrode; g, glass tubing.

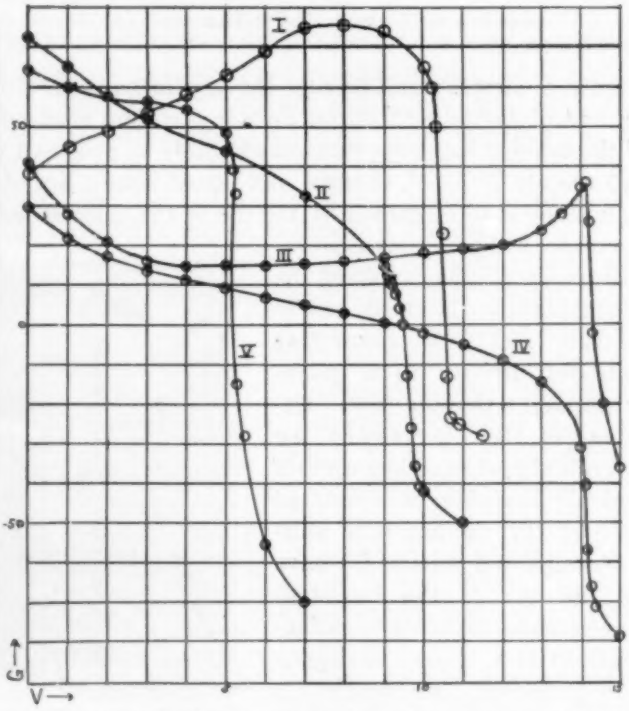


Fig. 4.—Titration Curves.—G, galvanometer readings; V, millimeters of reagent; I, hydrochloric acid with sodium hydroxide. Graphite-platinum electrodes. II, acetic acid with sodium hydroxide. Graphite-platinum electrodes. III, Mohr's salt with potassium dichromate. Tungsten-platinum electrodes. IV, Mohr's salt with potassium dichromate. Silicon carbide-platinum electrodes. V, Iodine with sodium thiosulphate. Graphite-platinum electrodes.

Procedure.—A weighed sample is treated according to quantitative methods up to the titration stage. In the case of the ferrous compounds the sample is treated with 20 ml. of diluted sulphuric acid (1 volume sulphuric acid with 4 volumes of water) and 15 ml. of a sulphuric-phosphoric acid mixture (75 ml. sulphuric acid and 75 ml. phosphoric acid diluted with water to 500 ml.). Following this treatment the iron solution is diluted to 200 ml. with water. After immersing the electrodes in the solution the filament current is increased to 0.05 amperes and the galvanometer adjusted to obtain a deflection of 50 or 60 mm. For best results the galvanometer shunt should be completely eliminated before beginning the titration. Resistance R_2 should be used only to protect the galvanometer from sudden current changes while adjusting resistance R_1. After some practice the experimenter will have little trouble in obtaining the proper galvanometer reading prior to titration. The reagent is run into the titration cell, at first, several milliliters at a time, and then more slowly, as the equivalence point is reached, when galvanometer readings are taken

more frequently. During some titrations it may be necessary to readjust the galvanometer by means of resistance R_1, especially if an instrument with a small scale is used. Vigorous stirring of the reaction mixture is necessary and is best accomplished by a small motor stirrer. It is well to wait thirty seconds after each addition of reagent to allow the galvanometer reading to become constant. The end-point is characterized by a sudden large deflection, *i. e.*, dE/dV, the rate of change of the E. M. F. of the titration cell with a small change in concentration of the reagent, approaches a maximum. It was observed that concordant results could be obtained when using the graphite or silicon carbide electrodes if, after each titration, the electrodes were immersed in cleaning solution, followed by thorough washing with distilled water. This apparatus is being used at the present time in these laboratories for the titration of alkaloids. A report of the work will appear shortly.

SUMMARY.

1. The use of graphite-platinum, tungsten-platinum and silicon carbide-platinum electrode pairs with a vacuum-tube titration apparatus has been suggested and illustrated.

2. The apparatus has been applied to the titration of some ferrous iron compounds of the U. S. P.

REFERENCES.

(1) Goode, *J. Am. Chem. Soc.*, 44 (1922), 26; Calhane and Cushing, *Ind. Eng. Chem.*, 15 (1923), 1118; Treadwell, *Helv. Chim. Acta*, 8 (1925), 89; Williams and Whitenack, *J. Phys. Chem.*, 31 (1927), 519; Müller, *Trans. Electrochem. Soc.*, 62 (1932), 335; Furman, *Ind. Eng. Chem., Anal. Ed.*, 2 (1930), 213; Kolthoff and Furman, "Potentiometric Titrations," John Wiley & Sons, Inc., New York (1931); Taylor, "Treatise on Physical Chemistry," Van Nostrand Co., New York, 2nd Edition (1931).

(2) Brünnich, *Ind. Eng. Chem.*, 17 (1925), 631.

(3) Furman and Wilson, *J. Am. Chem. Soc.*, 50 (1928), 277.

(4) Kamienski, *Z. physik. Chem.*, 145 (1929), 48; 138 (1928), 345.

(5) Knop, *J. Am. Chem. Soc.*, 46 (1924), 263.

(6) Kolthoff and Sarver, *J. Am. Chem. Soc.*, 32 (1910), 539; 52 (1930), 4179; 53 (1931), 2906.

NOTE: The author takes this opportunity to thank the Globar Corporation and the Acheson Graphite Co. of Niagara Falls, N. Y., for the silicon carbide and graphite electrodes used in this work.

A NOTE ON THE ASSAY OF REDUCED IRON.*[1]

BY MARGARETHE OAKLEY AND JOHN C. KRANTZ, JR.

INTRODUCTION.

Reduced iron has found a place in practically all of the pharmacopœias of the world. In some, the evaluation is expressed in terms of metallic iron and in others, the total iron content is employed. Winter (1) reviewed these various standards in 1913. The eighth revision of the United States Pharmacopœia employed the iodimetric process of assay. The ninth and tenth revisions employed the well-known mercuric chloride method. The British Pharmacopœia specifies the copper sulphate procedure; this method depends upon the displacement of the copper by the iron. In all of these methods, the ferrous or ferric oxide present in reduced iron remains unattacked by the reagents employed. In 1909 Frerichs (2) reviewed

* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] From the Bureau of Chemistry, Maryland State Department of Health.

the various assays and recommended the copper sulphate method on the basis of its being capable of a greater degree of precision.

Owing to the fact that this method has been continued in the British Pharmacopœia of 1932, in which only 80 per cent of metallic iron is required, the authors decided to investigate the method and compare it with that of the U. S. P.

EXPERIMENTAL.

Three commercial grades of reduced iron were mixed and sifted through a number 100 sieve. Assays were conducted by the method recommended for the U. S. P. XI and by the following modification of the method of the British Pharmacopœia. The difference between the U. S. P. X and U. S. P. XI methods lies in the fact that in the latter the mercuric chloride solution and reduced iron are heated together on a water-bath for ten minutes instead of boiling for five minutes.

The modified British Pharmacopœia method is as follows:

"Transfer to a 100-cc. volumetric flask about 0.6 Gm. of reduced iron accurately weighed. Add 30 cc. of copper sulphate T.S. heated to its boiling point. Shake the mixture frequently and vigorously during ten minutes. Cool to 25° C. and add sufficient distilled water to make 100 cc. Mix thoroughly and filter. To exactly 25 cc. of the filtrate, add 20 cc. of diluted sulphuric acid and titrate with tenth-normal potassium permanganate. Each cc. of tenth-normal potassium permanganate corresponds to 0.005584 Gm. of Fe."

The results obtained on the same sample of reduced iron by each of the two methods are shown in Table I.

TABLE I.

No.	Modified B. P. Method.	U. S. P. XI Method.
1	98.30	93.85
2	99.02	95.58
3	99.01	94.55
4	98.62	95.90
5	98.38	95.43
6	98.31	95.38
7	98.85	94.78
8	98.30	96.30
9	98.18	95.50
10	98.32	...
11	98.90	...
12	98.48	...
13	98.00	...
14	98.30	...
Mean	98.49	95.25

The probably error of a single determination of the modified British process calculated by the formula P.E. $= \pm 0.6745\sqrt{\frac{\sum v^2}{(n-1)}} = 0.23$ per cent. By the U. S. P. XI process the probable error is ± 0.48 per cent.

Obviously the modified British process is less cumbersome than the mercuric chloride method and according to the analysis of the data set forth has advantage of a higher degree of precision. The difference between the mean of the two determinations is approximately 3 per cent. Since the purity of the substance is based upon the elementary iron content, it is manifestly important to determine which of the two procedures more closely approximates the theoretical value.

In order to determine the absolute accuracy of the two methods a sample of powdered electrolytic iron was obtained through the courtesy of Dr. George D. Beal. This iron assayed between 99 and 100 per cent by direct titration with potassium permanganate after acid solution.

With the sample of pure iron both the U. S. P. and the modified British methods gave results between 99 and 100 per cent.

A sample of iron was prepared by thoroughly mixing 95 parts of powdered electrolytic iron with 4 parts of ferric oxide, 0.5 part of ferrous sulphide and 0.5 part of ferrous phosphide. This mixture containing 95 per cent of metallic iron was submitted to analysis by both methods.

The results obtained on this adulterated sample are set forth in Table II.

TABLE II.

No.	Modified B. P. Method.	U. S. P. XI Method.
1	98.11	95.10
2	97.57	94.71
3	96.85	96.56
4	98.09	95.17
5	97.28	94.60
6	94.75	94.20
7	97.95	...
8	94.18	...
9	98.00	...
10	98.40	...
11	98.20	...
12	98.20	...
13	98.72	...
14	98.42	...
Mean	97.48	95.06

It is obvious that in the presence of these impurities the modified method of the British Pharmacopœia fails to give results which correspond closely to the absolute content of elementary iron.

CONCLUSION.

1. The presence of ferric oxide, ferrous sulphide and ferrous phosphide in a sample of reduced iron vitiates the results obtained by the copper sulphate method. The mercuric chloride method gives absolute values in the presence of these impurities.

BIBLIOGRAPHY.

(1) Winter, P. E., JOUR. A. PH. A., 2 (1913), 296.
(2) Frerichs, G., *Merck's Report*, July (1909), 165.

ASSAY METHODS FOR SALTS OF ORGANIC ACIDS.*

BY RICHARD M. HITCHENS.

The assay methods for alkali salts of organic acids have been for many years the subject of much discussion. A survey of the problems involved is given by Clark.[1]

* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] Clark, JOUR. A. PH. A., 15 (1926), 6.

The customary method of assay has been to ignite the salt to sodium carbonate which is determined by titration with standard acid. This method is subject to many sources of error; it is tedious and time-consuming. Ignition to sodium sulphate or to sodium chloride, which are determined gravimetrically, has been used by some investigators. Still others have isolated the acid by extraction and determined the acid gravimetrically or volumetrically. All of these methods require considerable time and are subject to many sources of error.

In 1927, Henville[1] described a new method of determining the cation in sodium salicylate and sodium benzoate. His method consists of direct titration of the aqueous solution of the salt with standard acid to a methyl orange end-point in the presence of diethyl ether to extract the organic acid as it is liberated. At a methyl orange end-point the solution is extracted with a fresh portion of ether and the titration continued to a second methyl orange end-point which is not affected by further extraction with ether.

Such a method is simple, direct, rapid and accurate. It furnishes the same information as does the conversion to sodium carbonate, sulphate or chloride but with a higher degree of accuracy and in a much shorter time.

The method was adopted by the 1932 British Pharmacopœia as an assay method for sodium benzoate and sodium salicylate except that bromphenol blue indicator was substituted for methyl orange.

In an attempt to simplify the method still further, Krantz and Schmidt,[2] working on the official monograph for United States Pharmacopœia XI, decreased the volume of the aqueous layer, increased the volume of diethyl ether and discarded the second extraction. As stated by Henville,[1] this procedure is valid for sodium benzoate, the end-point after the first extraction agreeing closely with that after the second. With sodium salicylate, however, the first end-point is somewhat indistinct and gives low results. Different analysts in this laboratory disagree as much as 0.5% on the first end-point, their results ranging from 99.0–99.5% on pure sodium salicylate. After the second ether extract the analysts agree well, obtaining values of from 99.8–100.0%.

By the proposed U. S. P. XI method, even pure sodium salicylate would assay only 99.5% as a maximum. It would seem advisable for the method of the U. S. Pharmacopœia to be revised, whereby two extractions are made, thus giving quantitative results. This should present no difficulties since the extra step is simple and rapid and requires no special equipment. The whole analysis may be completed in ten minutes.

The simplicity and accuracy attained by the Henville method for the assay of sodium benzoate and sodium salicylate suggests its adoption for other salts.

Although the method has been suggested only for these two salts it is in reality a general method of assay. Consider a salt MA. The reaction

$$MA + HCl \longrightarrow MCl + HA$$

can be carried to completion provided the following conditions are fulfilled:

(1) HA is sparingly soluble in water and readily soluble in some solvent immiscible with water.

---

[1] Henville, *Analyst*, 52 (1927), 149.

[2] Krantz and Schmidt, Jour. A. Ph. A., 52 (1933), 953.

(2) HA is not too strong an acid, Ka less than about 2.5×10^{-3}. If much stronger than this, complete liberation of the acid at a p_H value of 4, the methly orange end-point, can scarcely be effected without an excessive number of extractions.

(3) MOH is a base, the dissociation constant of which is greater that 10^{-6}. If lower, the end-point, where MCl alone is present in the aqueous layer, will occur in too acid a solution for accurate determination of the end-point.

(4) The salts MCl and MA are water-soluble and insoluble in the immiscible solvent.

Any such salt MA, therefore, can be assayed by this method if a suitable solvent can be found for the acid HA, if HA is fairly water-insoluble and not too strong, and if the base MOH is not too weak. The choice of solvent, the indicator and the number of extractions necessary will depend upon the salt in question.

Sodium benzoate conforms well with these specifications. With Ka = 7×10^{-5}, at a p_H value of 4, about 30% of the benzoate remaining in the aqueous layer will be present as sodium benzoate, the rest as benzoic acid. Benzoic acid is readily ether-soluble and only slightly water-soluble. From solubility data one would expect about 500 parts of benzoic acid in the 75 cc. ether layer present in the U. S. P. XI analysis to one part in the 20-cc. aqueous layer, or that the first end-point would be about 0.2% low. Thus one ether extraction should be sufficient. This is verified by experiment.

Sodium salicylate is slightly different. The dissociation constant of salicylic acid is about 1×10^{-3}. Thus at a p_H value of 4, only 20% of the salicylate in the aqueous layer is present as salicylic acid; the remainder is sodium salicylate. From solubility data there should be about 600 parts of salicylic acid in the ether layer per one part in the aqueous layer. But there are four parts of sodium salicylate per one of salicylic acid so that the combined salicylates in the aqueous layer may amount to 0.8% of the original sample. The first end-point will be low by this amount. A second extraction is necessary to remove the last traces of salicylates. This is borne out by experiment.

Ammonium benzoate and salicylate may be assayed by this method; the same arguments hold as for the sodium salts. The correct indicator would be methyl red. Unfortunately this dissolves in the ether layer. Methyl orange, however, gives results only 0.05% high, well within the limits of accuracy of the method.

The method is applicable to other salicylates such as magnesium, zinc, strontium.

It is applicable also to sodium barbital. Barbital has an acid dissociation constant of about 10^{-7}. Thus at a p_H value of 4, practically complete liberation of barbital has occurred, only 0.1% of the barbital remaining in the aqueous layer being present as sodium barbital. Even though fairly water-soluble and only moderately ether-soluble, one ether extract should be ample to give quantitative results.

It is applicable also to sodium phenobarbital. Phenobarbital has an acid dissociation constant of about 4×10^{-7}. Thus at a p_H value of 4, 0.4% of the phenobarbital in the aqueous layer is present as the sodium salt. Since phenobarbital is only slightly water-soluble and readily ether-soluble, one extraction should give quantitative results.

The method was tested experimentally on the above salts.

Materials.—Sodium benzoate and salicylate, U. S. P. products dried to constant weight at 100° C. Ammonium benzoate and salicylate U. S. P. dried to constant weight over solid sodium hydroxide. Strontium salicylate U. S. P., magnesium salicylate, zinc salicylate, all hydrates and not dried before use. Sodium barbital U. S. P. dried to constant weight at 100° C. Sodium phenobarbital N. N. R. dried to constant weight at 140° C., according to the instructions of N. N. R.[1] and A. D. M. A.[2]

Reagents.—Diethyl ether U. S. P. was found to be sufficiently neutral without further treatment. *N*/2 hydrochloric acid was standardized gravimetrically by precipitation as silver chloride.

The procedure was essentially that of Krantz and Schmidt[3] except that after the first end-point had been reached the aqueous layer was drawn off through a separator into a second flask, 20 cc. of ether added and the titration continued until a second methyl orange end-point was reached.

The results are tabulated below. The first column states the salt titrated, the second the assay after one extraction, the third the assay after two extractions. Each analysis refers to a different sample of the salt.

Salt.	Assay after One Extraction.	Assay after Two Extractions.
Sodium benzoate	99.5%	99.7%
	99.6	99.8
	99.7	99.8
Sodium salicylate	99.5	100.0
	99.2	99.8
	99.2	99.9
Ammonium benzoate	99.0	99.2
	99.2	99.4
(by ammonia evolution)		99.1
		99.3
Ammonium salicylate	98.6	99.4
(by ammonia evolution)		99.4
Strontium salicylate,	98.9	99.5
dihydrate	99.3	99.9
Magnesium salicylate,	99.1	99.8
tetrahydrate	99.0	99.6
Zinc salicylate, trihydrate	101.0	102.2
Sodium barbital	99.9	99.9
	99.8	99.8
Sodium phenobarbital	98.5	98.5
	98.5	98.5

It is evident that sodium and ammonium benzoate give almost quantitative results with one extraction.

All of the salicylates show the same type of results, the first end-point being at least 0.5% low, the second quantitative.

The magnesium, strontium and zinc salicylates are all hydrates. No attempt was made to dry them to the proper water content since the object in view was to determine the difference between the end-point after one and after two ether extractions. The magnesium and strontium salts apparently contain the correct amount of water of hydration. The zinc salt is slightly over-dried.

---

[1] "New & Nonofficial Remedies," American Medical Association.

[2] American Drug Manufacturers' Association, "Proceedings," 1933.

[3] Refers to footnote 2, page 12.

Sodium barbital gives quantitative results even with only one extraction. This would be expected on account of the weakly acidic nature of barbital.

The sodium phenobarbital gives low results even when dried at 140° C. This is in accord with the results of the A. D. M. A.[2] who found the salt to form a stable hydrate from which it was impossible to remove all the water even at 140° C. That this method does titrate quantitatively the cation in this salt is demonstrated in the following series of experiments.

As a further check on the method the following experiment was carried out on pure salicylic acid, benzoic acid, phenobarbital and barbital. A suitable weight was titrated directly with standard alkali to a phenolphthalein end-point. The water was removed by evaporating under reduced pressure. The resulting salt was titrated as above and the titration compared directly to that obtained by neutralizing exactly the same volume of sodium hydroxide with standard acid to a methyl orange end-point in the presence of ether. In this manner the effect of possible impurities in the commercial salts was eliminated, the problem being the quantitative recovery of the standard alkali added. Entirely analogous results to those in the above table were obtained. With phenobarbital and barbital quantitative recovery was obtained with one ether extraction; with benzoic acid within 0.2% on the first extraction and quantitative recovery on the second; with salicylic acid at least 0.5% low on the first extraction but quantitative recovery on the second. These experiments act as an independent check on the accuracy of the method.

CONCLUSION.

Henville's method for assay of sodium benzoate and sodium salicylate whereby the salt is titrated directly with standard acid in the presence of diethyl ether to a methyl orange end-point is a general method. It is applicable to water-soluble salts of the type MA where HA is an acid fairly insoluble in water and appreciably soluble in some solvent immiscible with water; where HA is not too strong an acid, apparent dissociation constant less than 2.5×10^{-3}; where MOH is not too weak, apparent dissociation constant greater than 10^{-6}.

The simplified assay method for sodium salicylate suggested by U. S. P. XI in which the end-point is taken after only one ether extraction, gives at least 0.5% low results, two extractions being necessary to give the correct assay.

LABORATORIES, MONSANTO CHEMICAL COMPANY,
ST. LOUIS, MO.

DIGITALIS ASSAY ON NORMAL AND EXSANGUINATED CATS.*

BY DAVID I. MACHT.

(WITH THE TECHNICAL ASSISTANCE OF M. B. MACHT.)

Pharmacologists in general recognize the cat method as the most useful means of assaying digitalis preparations. Variations crop up, however, even when this method is employed. To insure the most accurate and reliable data concerning

* From the Pharmacological Research Laboratory, Hynson, Westcott & Dunning, Inc., Baltimore, Md.

assay of digitalis, a knowledge of the different factors affecting or producing such variations is very desirable. A number of these have already been discussed by various authors. Van Wijngaarden has suggested a mathematical formula for calculating the most reliable figures obtained from a given series of cat experiments (1). Macht and Colson have found that there is a marked difference in the killing doses of digitalis for vagotomized and non-vagotomized cats, respectively (2). Furthermore, the present writer has discovered that meteorological conditions, and particularly sudden changes in the barometric pressure, must be taken into account when assaying digitalis on cats (3). In the present communication, another factor markedly influencing the toxicity of digitalis for cats is described.

In this laboratory, fresh arterial blood is often obtained from cats for assaying or determining the activity of heparin, which is manufactured on the premises. Healthy cats are anesthetized with ether for this purpose. One cannula is inserted into the carotid artery and another into the femoral vein. From 30 to 60 cc. of blood are drawn from the artery, and a corresponding volume of physiological saline is then injected into the animal through the vein. After this operation the animal is kept under anesthesia and used for some other physiological or pharmacological experiment. The author and his assistants found that when digitalis preparations were assayed on a cat in which blood (drawn off in the manner described above) had been replaced by physiological saline, the lethal dosage was much smaller than that required to kill a normal cat. The subjoined table exhibits the results obtained with five different lots of digitalis tincture assayed on normal cats, on the one hand, and on cats bled from one-half hour to one hour previously, on the other. In every case the animals were kept under light ether anesthesia;

TABLE INDICATING RESULTS OF ASSAY OF VARIOUS LOTS OF TINCTURE OF DIGITALIS.

	Normal Cats.			Exsanguinated Cats.		
Lot.	Weight of Cat in Kg.	M. L. D.—Cc. per Kilo of 1:10 Dilution.	Lot.	Weight of Cat in Kg.	Cc. of Blood Drawn.	M. L. D.—Cc. per Kilo of 1:10 Dilution.
A	3.0	10.1	*A*	3.0	60	6.2
	3.9	9.2		2.4	50	7.0
	3.0	10.8		2.4	45	7.5
	2.8	10.0		3.2	45	8.1
	3.4	10.0		3.2	60	7.9
B	2.9	14.2	*B*	2.5	25	11.6
	3.0	14.4		2.7	35	13.4
C	3.0	14.0	*C*	2.8	40	10.1
	2.7	14.0		3.0	55	7.3
	3.2	13.8		2.9	45	10.0
D	2.0	13.2	*D*	3.0	50	8.5
	1.9	12.0		3.2	55	9.0
E	3.3	14.9	*E*	3.1	65	12.5
	3.0	13.4		3.2	65	11.5
	2.9	14.4		3.2	60	11.9
	Grand average	12.6 cc.				9.5 cc.

and the tincture, diluted 1:10 with physiological saline, was injected through the femoral or saphenous veins according to standard methods at regular intervals. The minimal lethal dose required to kill an animal is expressed in cubic centimeters of the 1:10 dilution. It will be noted that, even when the amount of blood removed

was as little as 25 cc., the killing dose of the digitalis was smaller in the exsanguinated cats than it was in the normal animals. What the explanation of this phenomenon is the writer is not prepared to say. It is certainly not due to any irritation or injury to the vagus and sympathetic nerves in the neck because control experiments were made on animals in which these nerves and the carotid arteries were removed without subsequent bleeding of the animal. The difference in toxicity would seem to indicate that the active principles of digitalis may enter into some loose combination with the proteins of the blood and render them less potent, but this has not been definitely established. The writer has always found that the most reliable figures are obtained when the tests for digitalis are performed on cats weighing not less than 2 Kg. and not more than 3.5 Kg. The difference in the killing doses for exsanguinated and normal cats, respectively, is worthy of notice because the greater our knowledge of the factors responsible for variations in digitalis assay, the more reliable will be the figures obtained by investigators who take these factors into consideration.

REFERENCES.

(1) Van Wijngaarden, *Arch. exptl. Path. Pharmakol.*, 113 (1926), 40.
(2) Macht and Colson, *J. Pharmacol. & Exper. Therap.*, 9 (1916), 343.
(3) Macht, *Am. J. Pharm.*, 106 (1934), 135.

BALTIMORE, MD.

METHODS OF IDENTIFICATION OF THE RHIZOMES OF IRIS VERSICOLOR L. AND IRIS VIRGINICA L.*

BY GEORGE M. HOCKING.[1]

Most of the Blue Flag Root in commerce appears to come from the north- and central-eastern counties of Florida. The whole drug appears on the market in two forms, *viz.*, "with fibre" (*i. e.*, with the roots still attached to the rhizome) and "free of fibre" or "stripped." The species, *Iris versicolor* L., has always been named as the official source of the drug, Iris versicolor. Another species, *I. caroliniana* Watson, was recognized for the first time in the N. F. V, presumably on the basis of Farwell's statement (1) that in his twenty-five years' experience with crude drugs, Blue Flag Root had come almost entirely from this species. By the rule of priority, the name *I. virginica* L. takes preference over the name *I. caroliniana* Watson, and this revised nomenclature is used in this paper.

The statement is sometimes made (2), (3), (4) that Blue Flag Root is adulterated. Thus, Rusby (5), (6) says that this is probably the case to a large extent with Iris versicolor from the south-eastern states. In 1911, he (7) stated that much of the article appeared to come from *I. missouriensis* Nuttall, which is provided with a larger rhizome and was more readily and cheaply collected. The possibility of adulteration from this source now is remote since no Blue Flag seems to be collected in the areas where this species grows. In the south, collectors of and dealers in Blue Flag accept as genuine only the "red root," *i. e.*, the rhizome reddish when

* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] Instructor in Pharmacology, School of Pharmacy, The George Washington University.

broken across as opposed to "White Flag Root" which is whitish in section. Farwell[1] states that in forty years of crude drug handling he had never observed adulteration of Iris versicolor.

Small (8) groups *Iris versicolor* and *I. virginica* together with *I. Shrevei* Small[2] into the subgenus *Versicolores*. This closely related group of species is incorporated by Dykes (9) into the subgenus *Lævigata* of section *Apogon* of the genus, and this indicates a close kinship with the European *I. pseudacorus* L. so long known to materia medica. Members of subgenus *Versicolores* are distributed over eastern and central North America. Contrary to the statement which appears in many floras, *e. g.*, Small (8), *I. versicolor* does not occur throughout all of eastern North America, but is restricted to the area, roughly, north and east of a line between Washington, D. C., and northern Wisconsin (10). *I. Shrevei*, if it is to be regarded as a true species and not identical with *I. virginica*, occurs in the Mississippi Valley region, while in the broad strip of territory between, reaching from the Great Lakes in the north to Florida in the south, occurs *I. virginica*.

METHODS.

Because of the importance of Florida as a source of Blue Flag, methods were developed to distinguish rhizomes of the two most abundant Florida species, *viz.*, *Iris hexagona* Walter and *I. savannarum* Small from the somewhat less common species *I. virginica* and from *I. versicolor*, which latter does not grow naturally in the state. In addition, distinctions between the two official species were developed. According to Hume (11), the seven species of *Iris* native to Florida may be classified into three distinct groups comprising: (*a*) *I. tripetala* Walter; (*b*) *I. virginica* L.; (*c*) *I. savannarum* Small, *I. Kimballiæ* Small, *I. hexagona* Walt., *I. Albispiritus* Small, *I. rivularis* Small.

I. tripetala was the only type not studied, but this species is not one likely to provide adulteration since its rhizome is said (12) to be small and cordlike.

Fresh rhizomes of *I. hexagona*, *I. savannarum*, *I. versicolor* and *I. virginica* were obtained from plants identified by botanists specializing in the genus. The rhizomes were thoroughly examined macroscopically and microscopically, first fresh, then in the dried state. To facilitate sectioning and study, the dried rhizomes were immersed in 15% chloral solution for a few days. It was found possible to distinguish the rhizomes of official species and also to distinguish *between* them on the basis of three or more of the following points: (1) Dimensions; (2) Color (*a*) external, (*b*) internal, (*c*) extract in chloral solution, (*d*) with vanillin-hydrochloric acid, (3) Fracture; (4) Comparison of cortical and stelar radii; (5) Count of vascular bundles in cross section; (6) Breadth of vascular bundles; (7) Diameter of intra-endodermal parenchyma cells; (8) Odor.

In determining rhizome diameter, cortical and stelar radii, and vascular bundle numbers, pieces of average to maximum thickness rather than those of smaller size (which may be immature) must be selected, whereas for the remaining data, this precaution is unnecessary.

The eight characteristics enumerated above will now be taken up singly:

---

[1] Personal communication to author.

[2] Anderson (personal communication) regards *I. Shrevei* Small as at most no more than a variety of *I. virginica* L.

1. *Dimensions.*—Considerable variation exists in the length of pieces of the rhizome in commercial samples of the drug. Likewise, segmental and internodal dimensions are of little value since they vary greatly within the species and even for the individual plant because of varying environmental conditions.

Diametric values are of considerably more value in identification, although these again are affected by external conditions of growth. Of the group studied, *I. virginica* possesses by far the largest rhizome; only *I. savannarum* can compare with it in this respect, and the rhizomes of the two may be distinguished by other means.

AVERAGE MAXIMUM DIAMETERS OF FRESH* RHIZOME (IN MM.).

	I. versicolor.	*I. virginica.*	*I. hexagona.*	*I. savannarum.*
Vertical	16	24	11	12
Lateral	21	32	13	19

* Immersion of dried rhizomes in 15% chloral solution gives comparable values.

2. *Color.*—(*a*) A casual inspection of a sample of the drug from *I. virginica* gives the impression that the rhizome is distinctly reddish. A more careful examination, however, will show that *I. virginica* and *I. versicolor* are quite similar externally, but that in the former the rhizome has been sliced longitudinally (probably because of its large size), thereby exposing the bright reddish brown of the interior. The rhizome of *I. hexagona* is externally a rich reddish to dark purplish brown, that of *I. savannarum* similar but distinctly grayer.

(*b*) The rhizome of *I. versicolor* sectioned is dirty yellow to yellowish white to pale pinkish; that of *I. virginica* may be in places yellowish pink, but characteristically sections are dark red to purplish brown. In the other two species examined, sections are light yellowish, almost creamy white, and this is said to be true of the four remaining species of Florida iris (12).

(*c*) When macerated for several days in 15% chloral solution, the liquid takes on a dark reddish brown coloration with *I. virginica* but becomes no more than greenish yellow with *I. versicolor.*

(*d*) As discovered for *I. pseudacorus* by von Lingelsheim (13), the rhizome of *I. virginica* is colored a brilliant red when treated with vanillin and strong hydrochloric acid, while that of *I. versicolor* is stained a pale pink. The rhizome of *I. savannarum* is only slightly stained by the same reagent. This test might perhaps be extended to other non-official *Iris* species: if satisfactory, it would be particularly useful for the examination of the powdered drug.

3. *Fracture.*—With the exception of *I. virginica*, the fresh rhizome of Florida *Iris* species break with a snap leaving a clean fracture (12). The fracture of *I. virginica* and *I. versicolor* rhizomes is tough.

4. *Comparison of Stelar and Cortical Radial Values.*—In the table following, the cortical radius is expressed as a percentage of the total radius: minimum and maximum values were found and recorded.

(CORTICAL RADIUS/TOTAL RADIUS) × 100%.

	I. versicolor.	*I. virginica.*	*I. hexagona.*	*I. savannarum.*
Minimum	16%	21%	30%	29%
Maximum	26%	38%	45%	56%
Average	21%	29½%	37½%	42½%

It will be noted that the maximum value for *I. versicolor* is less than the minimum value for the non-official species, whereas for *I. virginica*, although the variation is greater and the higher values tend to overlap values for non-official species, nevertheless the average value is quite distinctly lower. There is sufficient difference in the values for the official species to be of service in distinguishing between them.

5. *Count of Vascular Bundles in Cross Section.*—The material, softened in 15% chloral solution, was cross-sectioned in thin slices and stained with basic fuchsin. Counting bundles was rendered easier and more accurate by mounting on a slide, cutting into several strips, and using a lens magnifying ten diameters.

AVERAGE TOTAL COUNTS OF VASCULAR BUNDLES.

I. versicolor	263	*I. hexagona*	181
I. virginica	240	*I. savannarum*	195

I. versicolor and *I. virginica* again show a relationship in the numbers of their vascular bundles, and have a distinctly higher count than in the other species examined.

6. *Dimensions of Vascular Bundles and Parenchyma Cells.*—The vascular bundles of *I. versicolor* and *I. virginica* are similar, both in size and composition, and are materially different from those of the non-official *Iris* species examined. The bundles in all were concentric, with the xylem forming a more or less complete ring around the phloem. In both official species, the individual elements making up the bundles, particularly the tracheae, are considerably smaller in cross-section and more numerous than those of the other species. Only the smallest diameter of a bundle, here called the breadth, was determined.

AVERAGE VASCULAR BUNDLE BREADTHS (IN MICRONS).

I. versicolor	340	*I. hexagona*	154
I. virginica	336	*I. savannarum*	152

This again graphically illustrates the resemblance of the official species, and indicates, by a more than 100% increase in vascular bundle diameter, how markedly they differ from the non-official species studied.

7. *Odor.*—The rhizome of *I. virginica* has a very distinctive and aromatic odor, somewhat resembling that of slippery elm; this distinguishes it from *I. versicolor*, in which the odor is slight and not distinctive.

APPLICATION OF METHODS.

The methods just outlined were utilized in the examination of six commercial samples of the dried Blue Flag Root purchased on the open market and of four specimens of the green plants obtained from field collectors who took care to select specimens of the form identical with that which they collected commercially. Three of the latter were identified from the flower as well as from the rhizome (numbers 7, 8, 10).

No. of Sample.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
							——— Fresh. ———			
Rhizome (mm.) aver. lgth.	...	76	115	76	75	56	...	...	...	...
Rhizome (mm.) max. diam.	26	21	22	22	20	19	25	27	28	19
(Cort. rad./tot. rad.) × 100%:										
Horiz.	32	20	17	30	21	16	21	22	30	34
Vert.	37	36	32	38	34	27	31	27	34	41
Aver.	34	26	23	34	28	20	26	25	32	38
Vasc. Bdle. Count	250	308	221	216	244	296	246	289	365	160
Vasc. Bdle. Brdth. (in μ)	238	330	194	295	285	389	305	227	250	190
Diam. intraendoder. parench. cells (in μ)	105	100	83	90	80	65	85	70	95	80
Color with vanillin-HCl	Deep red	Deep red	Deep red	Deep red	Deep red	Slight	Deep red	Deep red	Deep red	None

The foregoing data afford proof of the value of the methods used in determining identity in commercial samples of Blue Flag. The prime source of each crude drug sample was traced: it was found that four came from Florida (Nos. 1, 2, 3, 4), and one each from the Carolinas (No. 5) and from the middle west, possibly Indiana (No. 6). No. 6 was identified as from *I. versicolor;* the samples from the south as

from *I. virginica*, except in one instance (No. 3), where the article from a northern dealer was found admixed with some *I. versicolor*.

The green plants were obtained from four areas in northeastern Florida; three (Nos. 7, 8, 9) represented *I. virginica;* the fourth (No. 10) was probably *I. savannarum*. The dealer handling this probably did not supply any large firms.

DIFFERENTIATION OF IRIS VERSICOLOR AND IRIS VIRGINICA.

The monograph on Iris Versicolor, N. F. V, has been criticized because in it a single description is employed to describe the drugs from two species. Since they differ so markedly in some ways, it is preferable to describe them separately. The following description of the article as it occurs in commerce is suggested as sufficiently distinguishing:

Unground Iris Versicolor.—Rhizome frequently branched, often provided with remnants of flower stalk; segments markedly constricted and thickly developed at intervals, elliptical in cross section at the enlarged portions, cylindrical at the constrictions. Up to 10 cm. in length and 2 cm. in thickness; with an average length of 5 to 6 cm. and an average diameter of a little over 1 cm.; not ordinarily sliced longitudinally; outer surface grayish brown, obscurely annulated with darker colored markings of leaf bases alternating light and dark, the lower with numerous circular root scars, 1 to 2 mm. across, and sometimes root remnants, particularly at the enlarged portions of the rhizome; coarsely wrinkled longitudinally especially upon the upper surface; fracture short, somewhat spongy, the broken surface with yellowish white to pale pinkish brown central cylinder and pale purplish cortex, the central cylinder exhibiting whitish vascular bundles distributed throughout and surrounded by a distinct endodermis; radius of cortex approximately one-fifth of total radius. Odor slight, somewhat unpleasant; taste acrid and nauseous.

Structure.—A more or less exfoliating epidermal layer of suberized cells with brownish walls; a hypodermis of one to three rows of cells with uniformly thickened strongly lignified walls, some of which contain a reddish brown amorphous substance; a relatively narrow cortex of characteristic structure with ovoid or spherical parenchyma cells, large intercellular spaces, some of the parenchyma containing starch, others a reddish brown amorphous substance; an endodermis of a single layer of cells with walls lignified and thickened on the inner and radial surfaces; a central cylinder made up of numerous nearly spherical parenchyma cells, between which are intercellular spaces not as large as those in the cortex; concentric vascular bundles occasional in the cortex, more numerous in the parenchyma of the central cylinder, mostly grouped toward its periphery; between 250 and 300 vascular bundles in cross section of rhizome, individual breadths averaging 340 microns.

Tests for Identity.—In contact with chloral solution, this is colored no more than a greenish yellow; when the powdered drug is treated with vanillin and strong hydrochloric acid, it is colored a faint pink.

Unground Iris Virginica.—Mostly simple, branching much less common than in *I. versicolor*, up to 20 cm., on an average about 8 cm., in length, and averaging 1 cm. in thickness; segments separated by enlargements not as pronounced as in *I. versicolor;* cut into longitudinal pieces by halving or quartering; many broken pieces; outer surface grayish brown to purplish brown, but sectioned surfaces pinkish brown to dull red to purplish brown, giving entire drug a reddish appearance; more deeply annulated than in *I. versicolor*, the upper surface with prominent markings of leaf bases and often showing their fibrous remains, the lower with numerous root scars; fracture short and brittle, the broken surface light to dark reddish brown to dark purplish brown; outer portion of cortex sometimes yellowish; radius of cortex approximately three-tenths of radius of rhizome. Otherwise similar to *I. versicolor*. Odor pronounced, aromatic, reminiscent of slippery elm; taste acrid, astringent, disagreeable, leaving hot sensation in throat.

Structure.—Similar to that of *I. versicolor*. Vascular bundles of similar size, but somewhat less abundant, with an average count of 240 in cross section.

Tests for Identity.—In contact with chloral solution, this is colored a dark reddish brown; when treated with vanillin and strong hydrochloric acid, the powdered drug is colored a brilliant red.

CONCLUSIONS.

1. In revising them onograph for Iris Versicolor, N. F. V, the name *Iris caroliniana* Watson should be replaced by that of *Iris virginica* Linné which is more acceptable by the rule of priority.

2. It is suggested that the section describing Iris Versicolor, N. F. V, be revised so as to distinguish between the drug from the species *Iris versicolor* L. and *I. virginica* L.

3. In order to distinguish the official from spurious species of *Iris*, it is necessary to include in the monograph more specific histological data, in particular, vascular bundle counts and dimensions, and stelar and cortical ratios, and in addition, color of the drug and color reaction with vanillin and hydrochloric acid.

4. Iris Versicolor from the southeastern United States does not seem to be generally adulterated at the present time.

REFERENCES.

(1) Farwell, Oliver A., *Bull. Pharm.*, 33 (1919), 475.
(2) Ricketts, Helen E., *Bull. Amer. Iris Soc.*, No. 3 (1921), 27, 28.
(3) *Idem.*, *Les Iris Cultivés*, I (1923), 175–183.
(4) Lloyd, J. U., *Pharm. Rev.*, 23 (1905), 330.
(5) Rusby, H. H., Bliss, A. R., and Ballard, C. W., "The Properties and Uses of Drugs" (1930), page 310.
(6) *Idem.*, *The Messenger*, 6 (1929), 238.
(7) *Idem.*, *Pharm. Era*, 44 (1911), 94.
(8) Small, J. K., "Manual of the Flora of the Southeastern United States" (3rd Edition, 1933), page 337. Excerpt.
(9) Dykes, W. R., through Diels, L., in A. Englers" Die natürlichen Pflanzenfamilien," Band 15a (1930), S. 501.
(10) Anderson, Edgar, *Ann. Mo. Bot. Gard.*, 15 (1925), 241–332.
(11) Hume, H. Harold, *Bull. Amer. Iris Soc.* (April 1933). Reprint.
(12) *Idem.*, Native Iris Rhizomes (MS. in edit.) (*ca.* 1933).
(13) von Lingelsheim, A., *Apoth.-Ztg.*, 44 (1929), 1314, 1315.

A STUDY OF A NEW SERIES OF URETHANES.*

BY W. A. LOTT AND W. G. CHRISTIANSEN.

As reported in another article, the authors have studied the hypnotic potency of amides and ureides whose acyl residues contain the characteristic grouping:

$$C_6H_5—CH = \underset{\displaystyle R}{\overset{\displaystyle |}{C}} —$$ (where "R" is an alkyl group)

In order to completely evaluate the grouping in this respect, it was decided to introduce it also into carbinol residues of urethanes; the carboxy group of acids from which the amides (and ureides) are derived being replaced by the carbinol —CH_2OH group. The general formulas for the amides and the corresponding urethanes are as follows:

Amide— $C_6H_5—CH = \underset{\displaystyle R}{\overset{\displaystyle |}{C}}—CONH_2$

Urethane—$C_6H_5—CH = \underset{\displaystyle R}{\overset{\displaystyle |}{C}}—CH_2O.CO.NH_2$

---

* Scientific Section, A. PH. A., Washington meeting, 1934.

Two such urethanes (carbamates) were prepared and tested for hypnotic activity against rats; they were found to be inactive.

EXPERIMENTAL.

1. *2-Methyl Cinnamyl Urethane.*—14.8 Gm. (0.1 mol.) of 2-methyl cinnamyl alcohol was dissolved in dry benzene and treated with a 24% benzene solution of phosgene containing 9.9 Gm. of phosgene; the latter was added dropwise with mechanical agitation, and external cooling. The initial temperature was 15° C.; it rose about 5° C. during this addition. After the temperature had fallen to 15° C., 12.1 Gm. of dry, freshly distilled dimethyl aniline dissolved in 50 cc. of dry benzene was added. This caused another moderate rise in temperature. After agitating for one-half hour to complete the reaction, the reaction mixture was washed several times with water, to remove the dimethylaniline hydrochloride. The benzene solution of the chloroformate was partially dried by shaking with anhydrous Na_2SO_4, filtered, returned to the flask equipped with the agitator and treated for one hour with a large excess of 28% aqueous ammonia. The benzene solution of the urethane was washed successively with water, dilute hydrochloric acid, 10% sodium carbonate and finally again with water. By this time a white crystalline product had already appeared in the benzene layer. It was collected by filtration. When the benzene filtrate was dried and concentrated, an additional quantity of the urethane crystallized.

About 12 Gm. of the crude material was obtained as snow-white crystals of melting point 130–131° C. After several recrystallizations from alcohol the product melted at 132–133°.

Assay: % Nitrogen found—7.46; calculated for $C_{11}H_{13}O_2N$: 7.33%.

2. *2-Amyl Cinnamyl Urethane.*—In an exactly analogous manner 2-amyl cinnamyl alcohol was converted to the corresponding urethane. In this case no product crystallized from the benzene solution until after it was dried, concentrated and chilled. From 19 Gm. of the alcohol about 11 Gm. of almost white crystalline product was obtained. After several recrystallizations from alcohol the product was snow white and melted at 77.5–78° C.

Assay: % Nitrogen found—5.60; calculated for $C_{15}H_{21}O_2N$: 5.66%. 7 Gm. of an oily by-product was obtained but not examined.

The alcohols from which these urethanes were prepared were obtained by reduction of the corresponding aldehydes using ethoxy magnesium chloride and the method described by Bogert and Powell (1). These authors also described convenient methods for the preparation of α-alkyl cinnamaldehydes (2).

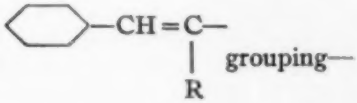
Biological tests with albino rats indicated that these two urethanes had no hypnotic action in doses up to 2 Gm. per kilo.

The biological tests on compounds reported herein were made in the Biological Research Laboratories of E. R. Squibb and Sons and we gratefully acknowledge their assistance.

SUMMARY.

1. Two examples of 2-alkyl cinnamyl urethanes were prepared and found to be lacking in hypnotic activity.

2. Since the urethanes in general are not rapidly hydrolyzed in the animal organism, it is to be concluded that either:

(*a*) no hypnotic activity resides in the  grouping—

or

(*b*) the above urethanes are not readily resorbed

Since in rats, the corresponding amides are active, the latter seems more probable.

REFERENCES.

(1) *J. A. C. S.*, 53 (1931), 1609.
(2) *Am. Perfumer and Essential Oil Rev.*, 25 (1930), 617.

RESEARCH DEPARTMENT OF THE CHEMICAL AND PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB AND SONS, BROOKLYN, N. Y.

THE ACTIVE CONSTITUENTS OF ERGOT: A PHARMACOLOGICAL AND CHEMICAL STUDY.*[1]

BY MARVIN R. THOMPSON.[2]

During 1929–1930, the writer published a series of ten reports embracing a review of the literature on Ergot and also the results obtained in certain pharmacological and chemical studies on Ergot and its more important pharmaceutical preparations. These reports presented evidence, in confirmation of a rather wide-spread unanimity of opinion, showing, among other things, that:

1. The amino-bases of Ergot (histamine, tyramine, cholines, etc.) could contribute little or nothing to the valuable therapeutic activity of the drug or any of its preparations.
2. The valuable therapeutic activity resided wholly in the "total specific alkaloidal fraction."
3. Of the four then known alkaloids, ergotinine and ergotaminine were comparatively inert, while both ergotoxine and ergotamine were indistinguishable in exhibiting intense activity by pharmacologic methods. Because of this great pharmacological activity, it was concluded that practically the full therapeutic activity of Ergot must reside in ergotoxine and/or ergotamine.
4. Aqueous Extracts of Ergot were practically worthless because they were invariably deficient in ergotoxine or ergotamine, and in addition were improperly standardized or not standardized at all.
5. Fluidextract of Ergot, U. S. P., or similar alcoholic or hydroalcoholic preparations, contained alkaloidal activity in satisfactory amounts and hence, such extracts were concluded to be superior to aqueous types of extracts.
6. Either ergotoxine or ergotamine was completely representative of the valuable pharmacological activity of Ergot, and, therefore, either of these alkaloids should be complete therapeutic substitutes for Ergot or its crude extracts.

Since publishing the above-mentioned reports, the author has continued to experimentally investigate certain phases of the ergot problem, largely because some of the most important conclusions regarding the activity and active principles of ergot have been based, by all workers in the field, upon experimental evidence of a much too indirect type, as for example, results obtained from experiments upon isolated uteri taken from non-pregnant and virgin animals. Such matters as absorption, changes in the uterus caused by pregnancy and the different stages of the œstrus cycle, and inherent differences in susceptibility between different animals, had been neglected by all pharmacologists up to 1930.

---

* Abstracted from a dissertation submitted to the Board of University Studies of the Johns Hopkins University, in conformity with the requirements for the degree of Doctor of Philosophy; reported in part before the Scientific Section of the annual convention of the AMERICAN PHARMACEUTICAL ASSOCIATION in Toronto, August 25, 1932, and in part at the annual meeting of the same body on May 10, 1934, at Washington, D. C.

[1] From the Department of Chemical Hygiene, School of Hygiene and Public Health, The John Hopkins University.

[2] Emerson Professor of Pharmacology, School of Pharmacy, University of Maryland; Consultant Pharmacologist, Food and Drug Administration, U. S. Department of Agriculture.

Of the conclusions drawn up to this time, the most important one requiring further confirmation in the way of more direct experimental evidence had to do with the active principles. Ergotoxine and ergotamine salts were being offered to the medical profession as full and complete substitutes for ergot or its crude pharmacopœial extracts. If these pure alkaloids were completely representative of ergot activity, there would be little justification for the continued use of the officially recognized crude extracts.

Earlier unpublished observations caused the writer to conduct a series of comparative experiments, using available salts of ergotoxine and ergotamine, and various crude extracts, for the purpose of determining whether or not the oxytocic effects of the purified alkaloids were actually the same as the effects produced by the crude extracts when administered to intact pregnant cats.

THE METHOD.

The afore-mentioned observations resulted in the selection of a method involving the use of pregnant cats because it was believed that of all experimental animals available for a large number of comparative experiments, the cat was the nearest possible approach to human conditions. For the adopted technique, anesthesia was necessary. Various barbituric acid derivatives such as nembutal, dial, amytal, phanodorn and phenobarbital, as well as ether, chloroform, chloretone and avertin have been used, but since all of these anesthetics were observed to depress uterine activity if the anesthesia became deep, and since pregnant cats vary considerably in their individual susceptibility to anesthetics, it was found distinctly advantageous to employ anesthetics which permit of intravenous administration so that the very cautious injection of divided doses could be carried out in such a manner that a relatively light anesthesia could be insured. The sodium salts of the shorter acting members of the barbituric acid derivatives were, therefore, used for most of the experiments. The use of inhalation anesthetics was abandoned in the beginning because they required an objectionable amount of constant attention, and also because respiratory irritation often caused decidedly objectionable coughing or sneezing during the maintenance of light anesthesia. A tracheal cannula was used to further avoid such disturbances. A somewhat heavier anesthesia, effected with ether, was usually employed during the operative procedure, but thereafter a lighter level of hypnosis was maintained.

Following anesthesia, the pregnant uterus was exposed, and the movements recorded upon the kymograph by the use of the movable arms of a myocardiograph, tying the arms into opposite ends of one of the more longitudinally contractile segments of one horn of the uterus. The animal was not immersed in a constant temperature bath, but a large electric warming pad was employed, and the small area of exposed uterus was constantly irrigated with Locke-Ringer solution at 37.5° C., the liquid dropping upon cotton partially covering the exposed part of the uterus. The entire procedure involves no hemorrhage.

A normal tracing was taken for approximately one-half hour or more in all instances before administering the ergot preparations. In the interpretation of the tracings reproduced in the illustrations of results obtained by this method, the relative magnitude of the recorded uterine responses cannot serve to show the actual relative intensity of the uterine activity produced by the different ergot preparations. The comparisons must be made with reference to presence or absence of response and *the rapidity of the onset of the response only*. The *magnitude* of the contractions in the different tracings is dependent, not alone upon the *intensity* of response induced by the ergot, but upon the contractility of the particular area of the uterus included between the two attached arms of the recording apparatus. Different uteri and different parts of the same pregnant uterus vary greatly in contractile power, and it was quite impossible to accurately judge the contractility at the time of attaching the recording apparatus. Some of the uteri showing the lowest magnitude of recorded response were observed to show a much greater actual response than other uteri which responded feebly but recorded enormous excursions of the writing lever on the kymograph. This could readily be noted simply by visual observations of the exposed uterus.

Using this technique, it is fully realized that the anesthesia and operative procedure results

in an "abnormal animal." The studies involved were, however, of a purely comparative nature, with the surgical procedure and anesthesia operating as a more or less cancellable constant. Nevertheless, to make this study as critical as possible, the effects of the various types of ergot preparations and chemical fractions or principles upon the strictly normal animal would obviously add to the significance of the results.

Accordingly, use was made of an observation that representative extracts of ergot cause abortion in pregnant cats with phenomenal regularity, regardless of the stage of pregnancy. The young are invariably born dead, not during the violent uterine activity caused by ergot, but following this activity by 6 to 24 hours. In the very terminal stages of pregnancy the young are occasionally born alive. This test is obviously not of an accurately quantitative nature, but considerable importance has been attached to it as indicating ergot "activity" or "inactivity" in the fundamental studies which follow.

COMPARISON OF THE ACTIVITY OF HYDRO-ALCOHOLIC EXTRACTS, AQUEOUS EXTRACTS AND AVAILABLE SALTS OF ERGOTOXINE AND ERGOTAMINE.

1. Pharmaceutical.—Suitable portions of 24 different lots of crude ergot, all assayed and found to be of U. S. P. potency or higher, were mixed together to yield a total of approximately 5 Kg. This material was ground and de-fatted by the U. S. P. method. An acid hydro-alcoholic fluidextract was prepared from 1 Kg. by the fractional percolation method described elsewhere by the writer (1), a method involving the use of no heat whatever. Percolation was continued until the combined percolates, when assayed by the modified (2) Broom-Clark method, exhibited an alkaloidal potency equivalent to 0.5 mg. of ergotoxine ethanesulphonate per cc. The volume of product was 3.790 liters. This product, designated as Fluidextract No. 360, was stored in the refrigerator at 0° to 5° C., small portions being removed for use as needed.

Another 1-Kg. portion of the same powder was converted into an Aqueous Extract exactly as above, except that water alone constituted the menstruum. Percolation was carried to the same volume as for the Fluidextract No. 360, *i. e.*, 3.790 liters. This product was designated as Aqueous Extract No. 361, and was stored in the same refrigerator as the Fluidextract No. 360. When assayed by the same method as the fluidextract, a potency equivalent to 0.19 mg. of ergotoxine ethanesulphonate per cc. was revealed. It will be noted that this was considerably less than half of the alkaloidal potency contained in the hydro-alcoholic fluidextract. *But it should also be noted that one cannot simply assume that aqueous extracts are alkaloid-free, even though they invariably contain less alkaloid than the hydro-alcoholic extracts.*

Both of the above extracts were also assayed by the U. S. P. Cockscomb method and by the colorimetric method of Smith (3). The writer, after several years of experience, holds little faith in the routine accuracy of the Cockscomb method unless an impossible number of birds are used. It may be stated, however, that both extracts gave satisfactory cockscomb reactions in agreement with the potency revealed by the more accurate Rabbit Uterus method. As to the colorimetric method, increased experience causes the writer to doubt the accuracy of the values originally obtained for the above extracts. Both extracts gave the color reactions, however, and the fluidextract, as by the other methods, proved to possess a higher alkaloid content than the aqueous extract. The colorimetric values were higher than the physiological values for both extracts. Studies relating to the color reaction and its quantitative value will be reported later. It is important

to point out that all three of these methods, which are believed to measure only alkaloidal activity, showed the presence of significant amounts of ergot alkaloids, even in the aqueous extract.

2. *Pharmacological.*—A number of experiments, recording the effects of oral doses of various ergot extracts as well as salts of ergotoxine and ergotamine upon the uterus of lightly anesthetized pregnant cats, showed beyond doubt that both aqueous and hydro-alcoholic extracts, as well as the commercially available salts of ergotoxine and ergotamine, were decidedly active in increasing the tonus and rhythmicity of the uterus. It was equally apparent that, viewing the results of four or more experiments upon each type of preparation, that the crude extracts, both aqueous and hydro-alcoholic, produced a uterine response which differed from that produced by either of the commercial alkaloidal salts. The chief difference was in the rapidity of the onset of response. Both of the above-described crude extracts acted much more promptly, usually well within ten minutes, and apparently more intensely than calculated equivalents of the ergotoxine and ergotamine salts. The effects of the alkaloidal salts developed only after 30 to 60 minutes. In these earlier experiments, the extracts were administered undiluted, the alkaloidal salts in 1:1000 dilution, all in 1- to 2-cc. oral doses by stomach tube.

Viewing all experiments, however, disturbing discrepancies were occasionally observed, particularly with respect to the promptness of action. The effects of the crude extracts usually developed within ten minutes, while the effects of the ethanesulphonate and phosphate of ergotoxine and the methanesulphonate and tartrate of ergotamine usually developed only after 30 to 60 minutes. But occasionally the effects of the crude extracts would be delayed until within the range of the time of action of the alkaloidal salts.

ABSORPTION FROM STOMACH AND INTESTINE.

Realizing that anesthesia has a depressant effect upon gastro-intestinal function, it was thought possible that the active principles of ergot might not be absorbed from the stomach, and that the passage of the small dose volume into the intestine was delayed, thus accounting for these discrepancies in the rapidity of onset of action. This posibility was then investigated.

In a series of 9 experiments upon pregnant cats, following the usual technique, pyloric ligations were performed before oral administration of the ergot preparation by stomach tube. In not one instance did the characteristic effects upon the uterus develop, even though ridiculously enormous doses of crude extracts were given (up to 10 cc. of the extracts) within two hours. Upon the removal of the ligature, after approximately two hours, an effect would manifest itself promptly, especially if a dose of 10 or 20 cc. of water were administered. A representative experiment is illustrated by the tracing in Fig. 1.

It appears quite obvious, therefore, that none of the active principles of ergot whether alkaloids or unknown substances, are absorbed to any significant extent from the stomach of the cat. Since the uterine activity could be made to manifest itself in no uncertain manner after removal of the pyloric ligature, it follows that absorption takes place from the small intestine. This was further confirmed in one experiment by leaving the pyloric ligature in place while a dose of 1 cc. of Fluidextract No. 360 was injected into the lumen of the small intestine by means

Fig. 1.—Cat: late pregnancy: uterus *in situ*. Time in minutes. Illustrating the lack of absorption of Ergot from the stomach and promptness of response of crude extracts following intestinal absorption. Pylorus ligated prior to administration of first oral dose of an Aqueous Extract known to be active. Note absence of oxytocic activity during two hours until ligature was removed, after which activity promptly developed. Hydro-alcoholic extracts in the same or even larger doses, likewise failed to show activity until the ligature was removed.

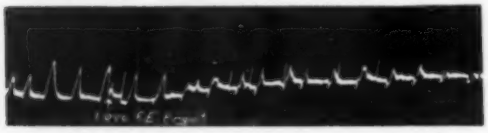


Fig. 2.—Cat: late pregnancy: uterus *in situ*. Time: Same as Fig. 5. The prompt (within ten minutes) response following the oral administration of 1.0 cc. of F. E. Ergot No. 360 plus water. The influence of respiratory movement is evident in this tracing. Magnitude of recorded contractions is low because of inclusion of only very small area of uterus between the two arms of the apparatus.

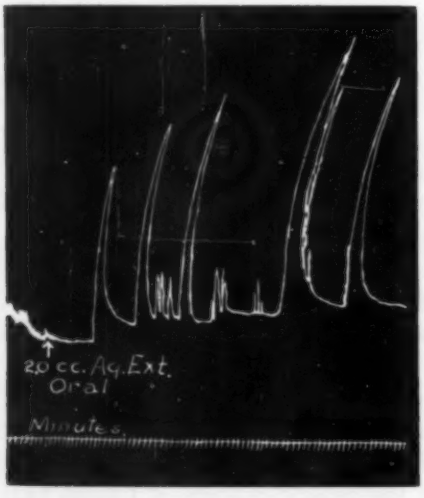


Fig. 3.—Cat: late pregnancy: uterus *in situ*. Prompt response following oral administration of 2.0 cc. of Aqueous Extract of Ergot with water.

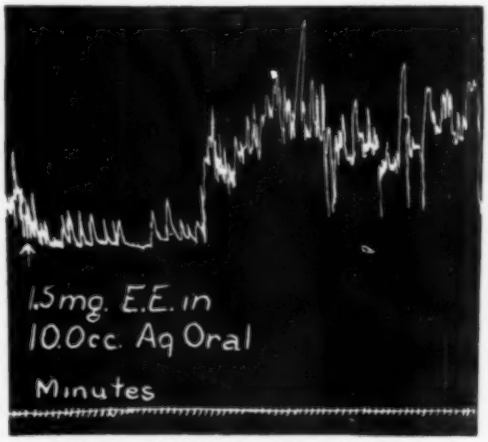


Fig. 4.—Cat: late pregnancy: uterus *in situ*. Delayed response following oral administration of large dose (1.5 mg.) of ergotoxine ethanesulphonate in 20 cc. water.

Fig. 5.—Cat: late pregnancy: uterus *in situ*. Time in minutes. The delayed uterine response following the oral administration of a large dose (1.0 mg.) of ergotamine methanesulphonate. After approximately one-half hour, however, pronounced activity is evident.

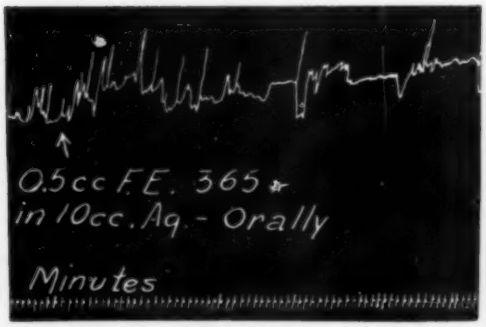


Fig. 6.—Cat: late pregnancy: uterus *in situ*. Prompt response following oral administration of 0.5 cc. of de-alcoholized F. E. No. 365 with water.

of a hypodermic needle. Uterine response resulted in $4^1/_2$ minutes, showing that intestinal absorption is quite rapid. Four similar experiments were performed using ergotoxine ethanesulphonate and ergotamine tartrate instead of a crude extract (two experiments upon each salt). No uterine effects were noted in any case within two hours while the pyloric ligation remained, even though the oral dose was 5 mg. in each case. Upon removal of the ligature, and administration of 20 cc. of water, uterine response developed only after 30 to 60 minutes, again revealing a great difference between these alkaloidal salts and the crude extracts. The effects produced by ergotoxine and ergotamine were indistinguishable by this method of study.

Because the comparative rapidity of onset of uterine action itself, following ergot administration into the gastro-intestinal tract, was the chief criterion to be used in distinguishing between the different constituents and preparations of ergot, it was necessary to use a procedure which would avoid the extremely variable delay in the passage of the dose from the stomach to the intestine. It was found that this variable could be satisfactorily removed by either of two ways. The drug could be injected directly into the lumen of the intestine, or the dose could be washed into the stomach with 10 to 20 cc. of warm water. The volume of water appeared to cause a fairly prompt opening of the pylorus in most instances, thus providing for a prompt transfer of the oral dose to the intestine for undelayed absorption. The animals were fasted for at least 12 hours before use.

DOSAGE.

The dosage administered to the cats was purposely large in practically all experiments. The method obviously has little quantitative value, but these studies were designed to simply determine presence or absence of oxytocic activity for various constituents and preparations of ergot, particularly with respect to type and promptness of action. The actual doses are indicated in the tables and illustrations.

DIFFERENCE BETWEEN NON-PREGNANT, PREGNANT AND POST-PARTEM UTERUS REGARDING RESPONSIVENESS TO ERGOT.

The use of non-pregnant cats was abandoned in the beginning of this investigation because the uteri of such animals responded only feebly or not at all, regardless of the size of the oral dose of either aqueous or hydro-alcoholic extracts of ergot. As a consequence the studies embraced in this report have involved the use of pregnant cats exclusively.

The cats used were those in which pregnancy was so far advanced that it could be readily detected by simple observation of abdominal distension or by palpation. While a considerable individual variation in sensitivity to ergot was observed, thus making observations rather obscure, the writer is left with the impression, after observing the uterine effects of ergot upon more than 250 cats in various stages of pregnancy and at various intervals post-partem, that the sensitivity or irritability of the uterus toward ergot increases as the pregnancy proceeds toward the termination of the gestation period. Greatest sensitivity to orally administered ergot appeared to be immediately preceding, during and immediately after, labor. After

TABLE I.—RAPIDITY OF ONSET AND INTENSITY OF UTERINE EFFECTS FOLLOWING ORAL ADMINISTRATION OF VARIOUS ERGOT PREPARATIONS TO LIGHTLY ANESTHETIZED PREGNANT CATS.

Type of Preparation.	Alkaloid Content.[1] Per cent	No. of Experiments.	Oral Dose.[2]	Average Time Required (Approx.) for Onset of Definite Uterine Effect. Minutes	Intensity of Uterine Effect.
Fluidextract, U. S. P.	0.050	6	2.0 cc.	6	Marked
Fluidextract, U. S. P.	0.120	2	1.0 cc.	6	Marked
Fluidextract, U. S. P.[3]	0.075	2	2.0 cc.	8	Marked
Fluidextract, U. S. P.[3]	0.03	2	2.0 cc.	8	Marked
Fluidextract, U. S. P.[3]	0.015	2	2.0 cc	4	Marked
Aqueous Ext. (Liq.)	0.019	6	2.0 cc	4	Marked
Aqueous Ext. (Liq.)	0.012	2	2.0 cc.	6	Marked
Aqueous Ext. (Liq.)	0.010	2	2.0 cc.	8	Marked
Tablets Ergotin, 3 grain[3]	0.000	3	20 tablets dissolved in water	No effect	None
Ergotin (Bonjean)[3]	0.125	2	0.5 Gm. in water	6	Marked
Ergotin (Bonjean)[3]	0.000	4	4.0 Gm. in water	No effect	None
Ergotoxine ethanesulphonate solution[4]	0.100	12	1.0 cc.	36	Doubtful to marked
Ergotamine tartrate solution[4]	0.100	15	1.0 cc.	38	Doubtful to marked
Histamine acid phosphate solution[4]		3	10.0 mg.	None	None
Tyramine hydrochloride solution[4]		2	100.0 mg.	None	None
Acetyl choline solution[4]		2	50.0 mg.	None	None

[1] Colorimetric method of Smith, in terms of ergotoxine ethanesulphonate.
[2] Washed in with 10 to 20 cc. of warm water, by stomach tube.
[3] Manufacturers label, age unknown.
[4] Solutions freshly prepared W/V; not assayed.

labor, the sensitivity appears to decline rapidly. By keeping a large number of pregnant cats on hand during the spring of 1932, it was possible to use two cats so nearly at term that true labor promptly followed the oral administration of 0.5 cc. of a U. S. P. Fluidextract of Ergot. Most powerful tonic uterine contractions started within five minutes in both cases, true labor developing in 35 minutes and 85 minutes, respectively. The uterine contents could not be expelled, of course, because of the abdominal incision. The violent abdominal muscular spasms forced uterus and contents through the incision to the exterior, throwing the recording apparatus out of adjustment and consequently ruining the kymograph tracings. Two other cats were used immediately after normal delivery was completed. A 0.5-cc. dose of U. S. P. Fluidextract, in two minutes for one and four minutes for the other, induced tonic contractions bordering on complete tetany. Uteri of cats used after the first day post-partem showed progressively decreasing sensitivity to ergot. After a week post-partem, the uterine response was observed to be very feeble, as in the case of the non-gravid uterus (3 experiments, 1 cat 49 hours post-partem, 1 cat 86 hours post-partem and 1 cat 196 hours post-partem). These few experiments cannot establish this important point conclusively, but if this general impression is correct even in part, there is a possibility that puerperal human patients may also gradually lose uterine sensitivity to ergot as the length

of the post-partem period increases. This may have some significance in studies similar to those of Moir (4, 5) in which the human patients are used not during the period when the action of ergot is most necessary and possibly most effective, but six days post-partem. In the specific studies of Moir, however, the point may be disregarded as far as the relative activity of different ergot preparations is concerned because his patients were all used at approximately the same post-partem interval. His comparative clinical evaluation of the different types of ergot preparations should, therefore, be perfectly valid. However, the possibility that all ergot preparations would produce a somewhat more intense effect than he observed, if given immediately at the termination of the third stage (when ergot is especially indicated), is a distinct possibility and is worthy of appropriate study.

WHAT ARE THE THERAPEUTICALLY ACTIVE PRINCIPLES OF ERGOT?

This investigation has furnished abundant confirmation of Moir's (4, 5) results showing that the commercially available salts of ergotoxine and ergotamine are possessed of oral activity, but that this activity falls far short of being wholly representative of the action of the drug itself or its crude extracts. It is evident, therefore, that there exists some unknown factor in the crude extracts. Typical tracings are shown in Figs. 2 for a Hydro-alcoholic Fluidextract, 3 for an Aqueous Extract, 4 for Ergotoxine Ethanesulphonate and 5 for Ergotamine Methanesulphonate. The tartrate and methanesulphonate of ergotamine exhibited the same indistinguishable type of delayed action. Table I presents a summary of the results of numerous experiments in which the uterine movements were recorded *in situ*. A highly important difference between the known alkaloids and the crude extracts becomes immediately evident upon examination of this table.

Fractionation of Ergot into Active and Inactive Components.

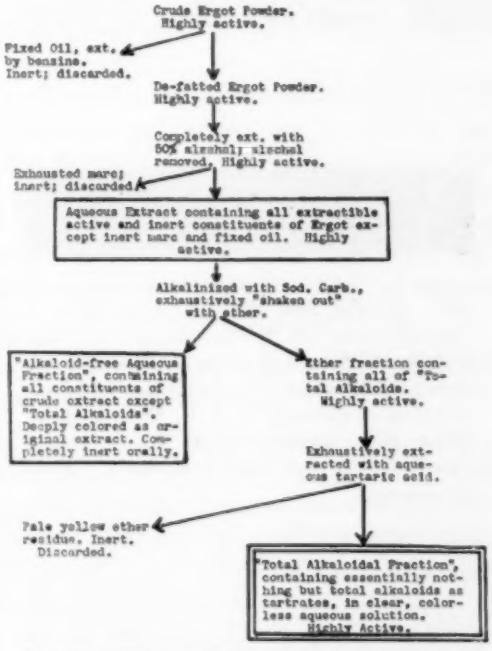

Crude Ergot Powder. Highly active.
Fixed Oil, ext. by benzine. Inert; discarded.
De-fatted Ergot Powder. Highly active.
Completely ext. with 50% alcohol; alcohol removed. Highly active.
Exhausted marc; inert; discarded.
Aqueous Extract containing all extractible active and inert constituents of Ergot except inert marc and fixed oil. Highly active.
Alkalinized with Sod. Carb., exhaustively "shaken out" with ether.
"Alkaloid-free Aqueous Fraction", containing all constituents of crude extract except "Total Alkaloids". Deeply colored as original extract. Completely inert orally.
Ether fraction containing all of "Total Alkaloids". Highly active.
Exhaustively extracted with aqueous tartaric acid.
Pale yellow ether residue. Inert. Discarded.
"Total Alkaloidal Fraction", containing essentially nothing but total alkaloids as tartrates, in clear, colorless aqueous solution. Highly Active.

Fig. 7.—Diagram of chemical fractionation procedure.

DISCUSSION OF TABLE I.

Considerable individual variation in these cats was noted. This was to be expected, because, entirely aside from a well-known individual variation in cats, it was obviously impossible to secure numbers of cats in the same stage of pregnancy. All were in advanced stages, however, because hair was well developed in the young in all cases (determined after sacrificing animals when experiment was terminated). Uterine effects of varying degrees of intensity were obtained from all preparations except the 3-grain ergotin tablets and one specimen labeled Ergotin (Bonjean). As observed by Moir on human patients, the salts of ergotoxine and ergotamine were decidedly less effective than the crude extracts, both as to promptness and intensity of effects, the alkaloids requiring 25 minutes or more, the extracts less than 10 minutes to produce their respective effects.

A significant difference between hydro-alcoholic and aqueous extracts was not revealed by this method in spite of the fact that the colorimetric method showed a higher alkaloidal content in the hydro-alcoholic extracts. It follows, therefore, that the aqueous extracts exhibited an activity entirely out of proportion to the alkaloid content, as observed by Moir in humans.

One decidedly interesting bit of information is furnished by these results. The only two preparations which proved totally inactive, even in ridiculously high doses, *were likewise the only two preparations for which a color reaction could not be obtained,* regardless of how much of each preparation was used for the color test. This point was critically investigated because the only two preparations failing to exhibit activity were those which actually proved to be completely alkaloid-free. It is very important to note that ergot preparations failing to give the color reaction, when the amount of preparation specified by Smith or by the B. P. Modification is used, actually need not be alkaloid-free. Good color reactions are obtained by this method only when the alkaloidal content of the preparation at least approximately approaches the level specified by the U. S. P. or the B. P. To prove actual freedom from alkaloids, approximately four or more times the usual amount should be used, the ether extract should be concentrated to less than the usual volume, and the acid aqueous extraction should likewise be reduced to about one-fourth the usual volume. Then when the reagent is added, and no color develops, one can conclude that the preparation is actually alkaloid-free for research purposes. These facts were kept in mind in obtaining the alkaloid values of Table I, the colorimetric readings being taken only when the intensity of color for standard and unknown was brought within plus or minus 20% of each other by using appropriate amounts of the preparations to be tested.

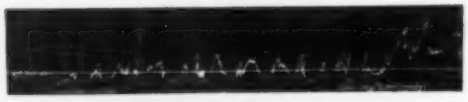


Fig. 8.—Cat: late pregnancy: uterus *in situ*. Showing lack of significant activity of "Alkaloid-free" F. E. No. 365 in very large oral dose (5.0 cc. with water). Note also the prompt and intense effect following the 2.0 cc. oral dose of the original F. E. No. 365 (from which the "Alkaloid-free F. E." was prepared), given over three hours later. Time in minutes.

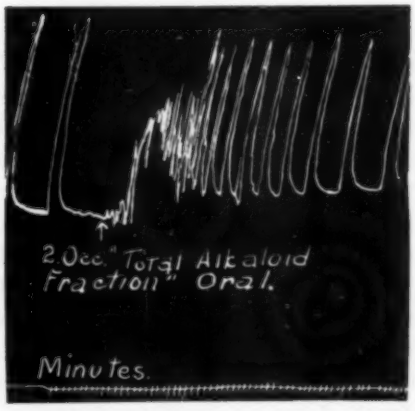


Fig. 9.—Cat: late pregnancy: uterus *in situ*. The prompt response following the oral administration of 2.0 cc. of "Total Alkaloidal Fraction" in 10 cc. water, prepared from F. E. No. 365.

Histamine, tyramine and acetyl choline did not contribute to the valuable activity of ergot preparations, as was concluded by the writer (6) in 1930, and by Moir (5) in 1932.

THE EFFECT OF ERGOT PREPARATIONS UPON NORMAL PREGNANT CATS.

Every ergot preparation included in Table I caused abortion within 36 hours in at least one pregnant cat, when given orally by stomach tube in large but non-lethal doses, *except histamine, tyramine, acetyl-choline and the two preparations which proved to be alkaloid-free.* The latter two preparations were without effect even in relatively enormous doses by either oral, subcutaneous or intramuscular administration, but those cats which failed to abort were subsequently (after three days or more) caused to lose their young by the administration of one of the other crude extracts or one of the salts of ergotamine or ergotoxine. Large necrotic abscesses were invariably produced by the subcutaneous administration of the larger doses of the crude extracts. By this method, therefore, it has been determined that the available salts of ergotoxine and ergotamine are decidedly active orally or parenterally. Likewise, hydro-alcoholic and aqueous extracts were decidedly active orally or parenterally unless they were alkaloid-free as determined colorimetrically. This method does not permit of a critical comparison between the salts of ergotoxine and ergotamine and the active crude extracts, because all induced abortion in an apparently similar manner.

Ten mg. of histamine acid phosphate, 50 mg. of tyramine hydrochloride or 20 mg. of acetyl choline, given individually or all in the same dose, by stomach tube, were ineffective in causing abortion (5 experiments).

The results of the investigation up to this point completely agreed with Moir's conclusion that the available salts of ergotoxine and ergotamine are not carriers of the full oxytocic activity of ergot. But inasmuch as it was possible to demonstrate the presence of alkaloids by their color reaction in every specimen which had proved active on either anesthetized or unanesthetized pregnant cats, it appeared quite probable that either the activity was completely due to the "total alkaloids" in some form or other, or else that the new unidentified non-alkaloidal "Moir principle" had disappeared with the alkaloids in the two inactive preparations.

THE DETERMINATION OF THE EXISTENCE AND CHEMICAL NATURE OF A NEW HIGHLY IMPORTANT SUBSTANCE IN ERGOT.

Extracts of ergot were prepared by using alcohol, ether, chloroform, acetone and other organic solvents. All preparations, administered after removal of the solvent, were active in varying degrees upon unanesthetized and anesthetized pregnant cats. The activity invariably proved to be of the "prompt new type" rather than the "delayed ergotoxine or ergotamine type." A 50% hydro-alcoholic menstruum proved to be decidedly the more efficient extraction menstruum. This information was of little aid, however, and considerable effort was then expended in isolating various pigments and other constituents for test. These efforts were apparently in the wrong direction since none of the fairly pure pigments or other non-alkaloidal constituents carried significant activity. The details of these unfruitful experiments will not be presented, because later work in a new direction completely ruled out the numerous pigments or colored constituents of ergot as carriers of oxytocic activity.

Observations up to this point appeared to justify the conclusion that a 50% hydro-alcoholic menstruum is capable of extracting every trace of active material from ergot if percolation is carried far enough. Such an extract, of course, contains much more inactive than active material, but it perhaps would provide the best starting point for the purpose involved. Accordingly, 1 Kg. of the defatted ergot powder described earlier in this report was subjected to exhaustive percolation with 50% alcohol by the fractional percolation method. Percolation was discontinued when the percolate could no longer be made to give the Smith color reaction. The

combined percolates were concentrated, without heat, under high vacuum to 1000 cc. The material was in contact with nothing but glass-ware at any time. The resulting deeply colored material was acid to litmus, and was essentially aqueous because all but traces of the alcohol had been removed during concentration.

This material was highly active as shown by its induction of abortion in three pregnant cats following 0.5-cc. oral dosage. It possessed the characteristic "prompt" type of oral activity as shown by three experiments upon lightly anesthetized cats, an example of which is illustrated in the tracing of Fig. 6. By the epinephrine-inhibition isolated rabbit uterus method, a total alkaloidal equivalent of 2.87 mg. ergotoxine ethanesulphonate per cc. was determined. This material was designated as Fluidextract No. 365.

It was reasoned that if the belief of Moir and Dale (5) that the total alkaloidal fraction did not carry the full activity of the drug were correct, the above fluidextract should show a great deal of activity after complete chemical removal of the alkaloidal fraction.

Complete removal of the "total alkaloids" was accomplished by slightly alkalinizing (to litmus) 500 cc. of the Fluidextract No. 365 by cautious admixture with finely powdered sodium carbonate, and exhaustively "shaking out" with many portions of ether, until the deeply colored aqueous fraction could no longer be made to yield the Smith color reaction, thus showing complete freedom from alkaloid. The deeply colored aqueous fraction was subjected to vacuum to remove residual ether. This alkaloid-free aqueous material, 500 cc. in volume, was designated as the "Alkaloid-Free Fraction."

The combined ether portions were concentrated to a volume of 500 cc., under vacuum without the aid of heat. All operations were carried out in the dark. The 500-cc. ethereal extract was then exhaustively extracted in a separatory funnel with many small portions of 1% aqueous tartaric acid solution until the Smith color reaction could no longer be obtained when final portions of the tartaric acid extract were reduced to one-fourth the volume and the aldehyde reagent added. The ethereal portion which had thus been completely exhausted of alkaloids, was placed under vacuum to remove the ether and the small amount of residue was incorporated in the "Alkaloid-Free Fraction."

The acid aqueous solution of the total alkaloids was reduced to a volume of 500 cc. by high vacuum, filtered and the small amount of precipitate (color negative) was incorporated in the "Alkaloid-Free Fraction." At this point the solution of total alkaloids still carried a pale yellow color. It was, therefore, purified by again alkalinizing with sodium carbonate and exhaustively shaking out with ether. The aqueous residue, after removal of the dissolved ether, proved completely inert on the uterus of both the anesthetized and unanesthetized pregnant cat in two divided oral doses totalling 50 cc., and was therefore discarded. The ethereal solution of the total alkaloids after reducing the volume to 500 cc. *in vacuo*, was washed several times with 0.5% sodium carbonate solution to remove most of the remaining pale yellow color. The sodium carbonate washings were unable to yield the color reaction and were completely inert, after neutralizing with HCl, upon oral administration to two pregnant cats in doses totaling 50 cc. These washings were therefore discarded. The washed ethereal solution of the total alkaloids was then again exhaustively extracted with small, divided portions of 1% aqueous tartaric

acid solution until all of the "total alkaloids" were contained in the acid aqueous solution (using the colorimetric test as the guide). The ether was again removed from the alkaloid-free ether fraction *in vacuo*, and the residue incorporated with the "Alkaloid-Free Fraction."

The purified aqueous tartaric acid solution was freed from dissolved ether and concentrated to 500 cc. *in vacuo* without heat, and filtered rapidly in the dark. The resulting product was absolutely clear and colorless. It should have contained essentially nothing but a solution of the "total alkaloids" of ergot in the form of their tartrates. This aqueous solution of the "total alkaloids" was designated as the "Total Alkaloid Fraction."

The diagram of Fig. 7 illustrates precisely what was done by the above chemical procedure to obtain the "Alkaloid-Free Fraction," containing essentially all of the extractives of ergot except the "total alkaloids," and the "Total Alkaloidal Fraction" which contained essentially none of the extractives of ergot except the "total alkaloids" in the form of their corresponding tartrates.

THE PHARMACOLOGIC ACTIVITY OF THE "ALKALOID-FREE FRACTION."

(*a*) *On the Cockscomb.*—Doses as high as five times the "threshold dose," or up to 3.0 cc. per Kg., failed to produce a cyanotic reaction in the combs of a series of ten cockerels meeting U. S. P. X specifications (as given under "Fluidextract of Ergot"). The "Alkaloid-Free Fraction" was, therefore, concluded to be inert by this method of test.

(*b*) *On the Isolated Uterus of the Virgin Guinea Pig.*—Activity equivalent to 0.15 mg. of histamine per cc. was determined by this procedure. The quality of activity was similar to that of histamine and was of a similarly transitory nature. The activity was entirely similar to that described earlier by the writer (7, 8).

(*c*) *On the Carotid Blood Pressure of the Anesthetized Dog.*—By intravenous administration, a transitory depressor effect similar to that produced by histamine was observed. The character of the tracings was essentially identical with those reproduced in an earlier publication (9). The amount of histamine-like activity was found to be, within the limits of experimental error, the same as observed on the isolated guinea-pig uterus.

(*d*) *By the Epinephrine-Inhibition Isolated Rabbit Uterus Method* (*2*).—No activity could be demonstrated by this method.

(*e*) *On the Uterus in Situ of the Anesthetized Pregnant Cat by Oral Administration.*—Using the same technique described earlier in this report, no uterine activity was observed in four experiments, even after a total of 50 cc. of the "Alkaloid-Free Fraction,' representing 50 Gm. of the original ergot, was administered to each cat during two and one-half hours. Each experiment was terminated after four hours or more by administering orally a dose of 1.0 cc. of the original unfractionated fluidextract. This produced significant uterine activity within ten minutes in each case, showing that failure of the "Alkaloid-Free Fraction" to induce activity was not due to unresponsive uteri. Illustrated by Fig. 8.

(*f*) *On Unanesthetized Normal Pregnant Cats.*—Oral doses up to 30 cc. failed to interrupt pregnancy in eleven cats. Two of the cats littered within four days after medication, but it is believed that the delivery was not brought on by the medication, as all of the young were born alive and fully developed. In abortion induced by large doses of ergot, the young are born dead unless the pregnancy is in the terminal stages. The cats appeared to remain free from any other symptoms following even the largest oral doses.

Subcutaneous doses of ten to fifteen cc. failed to interrupt pregnancy in eight pregnant cats. In the course of a week or ten days, enormous necrotic abscesses invariably developed around the site of injection. These abscesses healed with extreme difficulty, requiring the passage of many weeks before spontaneous healing was complete. Large scars remained after the healing.

It is concluded from the above pharmacologic studies on the "Alkaloid-Free Fraction" that no significant valuable uterine activity of any kind was contained

in this fraction. The pharmacodynamic activity observed upon the isolated guinea-pig uterus and upon the blood pressure of dogs is of a histamine-like character, is inactive orally, and contributes nothing of a desirable nature to the characteristic action of ergot.

This eliminates all of the deeply colored constituents as well as a large amount of other non-alkaloidal components of ergot as carriers of the activity of this drug. The fact that this fraction is completely inert upon the uterus of the pregnant cat, while still containing constituents capable of causing severe irritation in small doses and enormous slow-healing abscesses from large doses by parenteral injection, is an important observation. Complete exclusion of these constituents from ergot preparations intended for hypodermic use is very necessary. It is believed that the abscess formation is probably due simply to the non-dializable or non-absorbable nature of the material, thus creating an effect similar to that caused by any irritant, unabsorbable body inserted under the skin or into the muscle tissue.

THE PHARMACOLOGIC ACTIVITY OF THE "TOTAL ALKALOIDAL FRACTION."

(*a*) *On the Cockscomb.*—Following essentially the U. S. P. procedure in applying this method, using ergotoxine ethanesulphonate as the standard, this fraction was intensely active in causing cyanosis of the combs of ten cockerels. An activity corresponding to the equivalent of not less than 2.0 mg., and not more than 3.0 mg. of ergotoxine ethanesulphonate per cc. was determined.

(*b*) *On the Isolated Uterus of the Virgin Guinea Pig.*—This fraction was definitely active by this method. Doses of 0.02 cc. to 0.2 cc. in 100-cc. tissue chambers induced strong contractions. It was impossible to assign any definite value in terms of a standard because repeated dosage to the same uterine strips produced progressively decreasing responses, showing that the drug gradually induced a paralysis and that this effect could not be washed out with sufficient ease to permit of any accurate estimation. The action was similar to that described for ergotoxine, ergotamine and crude extracts in a previous report (7).

(*c*) *On the Carotid Blood Pressure of Anesthetized Dogs and Cats.*—A definite and prolonged pressor response was obtained in both dogs and cats by intravenous administration of 0.01 to 0.06 cc. per Kg. body weight. The response was indistinguishable from that illustrated in Figs. X and X-*a*, or as described for the "specific alkaloids" in an earlier report (9). Repeated dosage invariably led to a progressively decreasing response until the well-known "epinephrine-reversal" effect could be produced.

Oral doses of 1.0 cc., diluted to 20 cc. with warm water, failed to cause a significant change in the blood pressure of a cat. The pressor action, therefore, appears to be dependent upon the sudden appearance of relatively large amounts of the alkaloids in the circulation.

(*d*) *By the Epinephrine-Inhibition Isolated Rabbit Uterus Method* (*2*).—The potency by this method was found to be equivalent to 2.56 mg. of ergotoxine ethanesulphonate per cc. It will be noted that this value agrees fairly well with the value obtained, by the same method, for the original Fluidextract No. 365, from which this "Total Alkaloidal Fraction" was prepared. The difference in the two values is barely significant, and shows that the loss in alkaloidal activity sustained in the chemical fractionation procedure was not great.

(*e*) *On the Uterus, in Situ, of the Anesthetized Pregnant Cat by Oral Administration.*—After 31 experiments, following the technique already described, the writer is convinced that this "Total Alkaloidal Fraction," as well as three others prepared similarly, contained all of the significant characteristic uterine activity of ergot. The uterine effects usually developed well within ten minutes, differing from salts of ergotoxine or ergotamine in this respect. Figure 9 illustrates the promptness of action following oral administration of the "Total Alkaloidal Fraction." The promptness in action was indistinguishable from that observed following the administration of the original Fluidextract No. 365, from which this fraction was obtained. The promptness of action does, however, clearly show that the "total alkaloids" include a very important member in addition to ergotoxine or ergotamine.

(*f*) *On Unanesthetized Normal Pregnant Cats.*—The "Total Alkaloidal Fraction," in oral doses of 0.5 to 2.0 cc., interrupted pregnancy within 24 hours, in twelve cats in various stages of pregnancy. Subcutaneous or intramuscular doses of 0.25 cc. (4 cats by each injection route) likewise proved effective in terminating pregnancy. The young in all cases were born dead. Death of the cat occasionally resulted after abortion in experiments of this type, whether the preparation given was the "Total Alkaloidal Fraction," salts of ergotoxine or ergotamine, or any one of the active aqueous or hydro-alcoholic extracts. This was to be expected since most of the doses administered throughout this work were large.

The foregoing experiments upon the "Alkaloid-Free Fraction," and the "Total Alkaloidal Fraction," again demonstrate, as the writer previously concluded (7), that the isolated guinea-pig uterus method, as it is usually applied, is wholly unreliable as a means of evaluating the significant activity of ergot preparations, measuring chiefly the extremely variable and totally useless histamine type of activity rather than the alkaloidal activity.

GENERAL ANALYSIS OF RESULTS.

Moir's observations upon human patients to the effect that, given orally, both aqueous and hydro-alcoholic extracts of ergot produce a much more prompt and more effective uterine action than the available salts of ergotoxine or ergotamine, have been repeatedly confirmed in this study upon pregnant cats. It follows, therefore, that the crude extracts owe their superior activity either (*a*) to an entirely new unidentified substance as concluded by Moir, or (*b*) to a naturally existing unknown ergotoxine or ergotamine compound or combination differing from the available salts or ergotoxine and ergotamine, and which is more readily absorbed from the intestinal tract than the manufactured alkaloidal salts. The writer feels that "(*b*)" had to be considered as a possibility in spite of the fact that Moir believed his active aqueous extracts to be practically alkaloid-free, because evidence has been presented in this as well as in an earlier report (8) showing that such extracts, although containing a deficiency of alkaloids, are usually not actually alkaloid-free and that they may contain sufficient alkaloids to account for definite activity when administered to humans in large doses as used by Moir.

A further analysis of the present results, however, rather definitely rules out "(*b*)" as a possibility, because of the repeatedly demonstrated fact that the "Total Alkaloidal Fraction" contained every trace of the characteristic activity of the original quantitative de-alcoholized hydro-alcoholic extract. Specifically, this "Total Alkaloidal Fraction" could consist of essentially nothing but an acid solution of the "total specific alkaloids," and these obviously in the form of their corresponding tartrates. This should preclude the possibility that the crude extracts owed their superior oral activity to a "mysterious" salt, or combination, of the two important well-known alkaloids ergotoxine or ergotamine, in spite of the fact that neither of these alkaloids have ever been proved to exist as such, or as simple salts, in crude extracts or ergot itself.

This leaves only "(*a*)" as a possibility. Their possibility developed into a virtual certainty when it was observed that salts of ergotoxine and ergotamine fell far short of being completely representative of the "total alkaloidal" activity of ergot, and also that the only other known important pharmacodynamically active constituents, namely, histamine, tyramine and acetyl choline, were not responsible for any of the characteristic oral activity of the drug. It may be concluded,

therefore, that Moir's and Dale's belief that a new highly important unidentified substance exists in ergot and its crude extracts (both aqueous and alcoholic), is confirmed by these studies. Quite contrary to their apparent belief, however, this new substance is shown to behave characteristically as an alkaloid, since the studies here reported show the presence of this new substance in the completely colorless "Total Alkaloidal Fraction," while the "Alkaloid-Free Fraction" proved to be devoid of any oral or subcutaneous activity of any significant type. The writer, therefore, believes that this new substance must be classified chemically as a new member of the "total specific alkaloids" of ergot, and that the activity of aqueous extracts, observed by Moir in human patients, is to be ascribed to "residual alkaloid."

(To be continued.)

ANTIDOTES. I. GENERAL PLAN.*

BY JAMES C. MUNCH, AND F. E. GARLOUGH.[1]

Men from the earliest times have endeavored to find ways of relieving pain or injury to themselves by means of spirits, charms, mysticism, and later by use of herbs and animals. In these efforts they found some herbs and later extracts that were either beneficial or deadly. It was also observed that the animals were either beneficially or injuriously affected by certain plants or animals which they ate, as is reflected in the names—cowbane, sowbane and wolfbane which are plants poisonous to cattle, swine and wolves.

The fatal effects resulting from the bites of animals brought about the first real effort to find antidotes to poisons, though some earlier knowledge had been gained of the counter-action of one drug upon another. In Homer's "Iliad" describing the Trojan War and the adventures of ancient heroes (*Ca.* 1000 B.C.) many references are made to the wounds of the warriers being rubbed with a bitter, pain-assuaging root. Homer mentions 250 such cases. The earliest reference to a plant which was specifically believed to be an antidote for poison is found in Homer's "Odyssey;" "Moli" or "Molu" which is apparently a species of Allium (*Allium moly*). In this case Circe's potion was a form-transforming drug, the effects of which moly supposedly counteracted.

Among the earlier writers on antidotes was the Greek, Nicander of Colophon (185–135 B.C.), the Court Physician to Attalus, King of Pergamum, who made studies of poisons on condemned criminals, a common practice at that period. His first work, "Theriaca," which was written in Greek verse, had to do with the poisons of animal bite sand treatments of them. His second poem, "Alexipharmaca," tells of antidotes to poisons. In these he mentions twenty-two poisons, including aconite, cantharides, opium and conium. His chief antidotes include warm oil, mallow and linseed tea to excite vomiting.

The development of antidotes to poisons was greatly stimulated when, about the time of Mithridates (first century B.C.), poisons began to be extensively used

---

* Scientific Section, Madison meeting, 1933.

[1] Bureau of Biological Survey, Glen Olden, Pa., and Denver, Colo.

by certain ambitious or revengeful people to remove enemies or persons in the way of their personal advancement. The early effort was to develop a composite mixture of plant and animal materials that would protect against all poisons, bites of venomous animals and diseases. Several were put up in small cake or tablet form. A number of famous "theriaca," as the mixtures were called, were developed, containing from 37 to 250 ingredients guaranteeing protection. Mithridatium and two modifications of it were noted ones and appeared in the London Pharmacopœia as late as 1677 A.D. A red clay, "terra sigillata," which was excavated with much ceremony from a certain hill on the Island of Lemnos on August 6th of each year was given some attention. Tests in July 1580, showed that such a product saved the lives of dogs given lethal doses of mercury sublimate, aconite, apocynum or nerium! Subsequent reports of tests on condemned criminals, however, failed to show any more value for this product than for the unicorn's horn.

William Heberden (1710–1801) in his "Essay on Mithridatium and Theriaca" (1745) did much to expose the superstitions and worthlessness of these curious concoctions, and to banish them from the pharmacopœias. Antidotal studies since have been upon a more scientific basis.

A series of investigations have been made on various poisons by interested investigators. Some trials have been made on animals; some on humans. A great deal of information has been collected and has served as a basis for the preparation of various tables of antidotes. However, our search of the literature has failed to show any consistent study of several types of poisons under similar conditions. It was, therefore, deemed advisable to institute a detailed investigation along this line, with the hope of developing successful methods of treatment of men and animals.

Since the literature reveals enormous discrepancies in toxicity figures, we have repeated many determinations to establish authentic figures. Injections are given various laboratory animals, worms, fish, frogs, mice, rats, rabbits, cats and dogs by mouth, subcutaneously, intramuscularly, intraperitoneally or intravenously. We are also collecting recorded toxicological data for men.

Searches of the literature are being made to learn the suggested antidotes. Pharmacological and toxicological studies are made to serve as a rational basis for therapeusis. Based on this knowledge, the efficiency of various procedures for protecting against the fatal dose, and multiples of the fatal dose are being studied. Studies are being made of antidotal processes that may change the chemical nature of the poison, or prevent its absorption, or aid its elimination, or counteract its physiological effects, so as to save the life of a poisoned animal. In our present studies we are paying most attention to those poisons (strychnine, thallium, cyanides, arsenic and phosphorus), used in the control of noxious rodents and predatory animals.

CONCLUSIONS.

(1) Detailed searches of the literature are being made to determine the lethal doses of various poisons for men and animals; also their antidotes.

(2) Laboratory studies are being made to learn the value of various procedures suggested in the literature or developed in our work.

BIBLIOGRAPHY OF PHARMACEUTICAL RESEARCH

Compiled by A. G. DuMez, Reporter on the Progress of Pharmacy.

All articles in these lists will be presented in abstract form in the bound volumes of the Year Book, which is issued annually. Those desiring abstracts immediately can obtain them for a fee of one dollar each by communicating with A. G. DuMez, University of Maryland, School of Pharmacy, N. W. cor. Lombard and Greene Sts., Baltimore, Maryland.

Christie, John
Pharmacy in Soviet Russia
Chem. & Drug., 121 (1934), 642

PHARMACŒPŒIAS AND FORMULARIES.

Anon.
Practical Questions on the Swiss Pharmacopœia V
Schweiz. Apoth.-Ztg., 72 (1934), 732
Gardner, John H.
A note on the U. S. P. monograph on chrysarobin
JOUR. A. PH. A., 23 (1934), 1177
Potjewijd, T.
Review of the Hungarian Pharmacopœia IV
Pharm. Weekblad., 71 (1934), 1322
Potjewijd, T.
Review of the Jugoslavian Pharmacopœia 1933
Pharm. Weekblad., 71 (1934), 1385

APPARATUS AND MANIPULATIONS.

Anon.
A small tube-filling apparatus
Apoth.-Ztg., 49 (1934), 1607
Husa, William J., and Magid, Louis
Drug extraction. I. A study of various menstrua from the standpoint of swelling effects, penetration and extraction
JOUR. A. PH. A., 23 (1934), 1187
Konrich
On the application of the autoclave to sterilization in pharmacies
Apoth.-Ztg., 49 (1934), 1536
Rupp, E.
Small drying oven for analysis
Pharm. Ztg., 79 (1934), 1249
Zimmermann, W.
Drop bottle shapes and certainty of medicinal dosage
Apoth.-Ztg., 49 (1934), 1604

PHARMACEUTICAL PREPARATIONS.

Alpers, H.
Osterberg's Drops
Apoth.-Ztg., 49 (1934), 1625
Anon.
Waving and setting lotions
Pharm. J., 133 (1934), 653
Ansingh, E. W.
Difficulties with one per cent iodinated vaseline
Pharm. Weekblad., 71 (1934), 1388
Atkins, Frank
Pearliness in creams
Perf. & Ess. Oil Rec., 25 (1934), 332
Bartole, A.
Iodotannic syrup
Scienze farm., 1 (1933), 29; through *Chem. Abstr.*, 28 (1934), 3525
Bauer, K. H., and Junge, R.
On the knowledge of the scammony resins
Arch. Pharm., 272 (1934), 841
Bobranski, B.
Some remarks on the preparation and properties of "Mentholum valerianicum"
J. Pharm. et Chim., 20 (1934), 437
Brandrup, W.
On the application of pectins in pharmaceutical practice
Pharm. Zentralh., 75 (1934), 777
Brandrup, W.
Preparation of liniments with volatile oils
Pharm. Ztg., 79 (1934), 1262
Casparis, P.
Incompatibility of dimethylamino-antipyrine
Schweiz. Apoth.-Ztg., 72 (1934), 695
Clayton, W., *et al.*
Symposium on emulsions
Chem. & Drug., 121 (1934), 732
Merz, K. W.
Spirit of ethyl nitrite
Apoth.-Ztg., 49 (1934), 1553
Rothenkirchen, O.
On ammoniated liniment, D. A. B. VI
Pharm. Ztg., 79 (1934), 1194
Toni, Guiseppe
A new method for preparing tincture of strophanthus
Arch. farmacol. sper., 57 (1934), 161; through *Chem. Abstr.*, 28 (1934), 5595

PHARMACOLOGY, TOXICOLOGY AND THERAPEUTICS.

Anon.
Vitamin standardisation. Report of the Second International Conference
Pharm. J., 133 (1934), 594
Bodendorf, K.
Contribution to the history of local anesthesia in the *p*-aminobenzoic acid ester series
Apoth.-Ztg., 49 (1934), 1642
Freudweiler, R.
Organotherapy in pharmaceutical practice
Pharm. Acta Helv., 9 (1934), 216
Galloway, L. D.
Effect of oils, fats and waxes on antiseptic action
Mfg. Chemist, 5 (1934), 233–234; through *J. Soc. Chem. Ind.*, 53 (1934), 1036B
Hurst, Arthur F.
Dosage above the pharmacopœial maximum
Pharm. J., 133 (1934), 675, 703
Jurist, A. E., and Christiansen, W. G.
Fluctuations in the resistance of rats to neoarsphenamine as observed in routine toxicity tests over a period of four years
Jour. A. Ph. A., 23 (1934), 1171
Kanter, A. E., *et al.*
A new biologic test for hormones in pregnancy urine
J. A. M. A., 103 (1934), 2026
Kindler, K.
The significance of amines in chemotherapy
Arch. Pharm., 272 (1934), 811
Lingle, Robert M.
The assay of ointment of boric acid
Am. J. Pharm., 106 (1934), 421
Munch, James C.
Saliva tests. II. Heroin
Jour. A. Ph. A., 23 (1934), 1185
Regnier, M.-T.
Antitoxic power of glutathione in hydrogen cyanide poisoning
J. Pharm. et Chim., 20 (1934), 501
Rosen, Harry
The bioassay of squill
Jour. A. Ph. A., 23 (1934), 1180
Stieglitz, Edward J., and Knight, Alva A.
Sodium ferrocyanide as a clinical test of glomerular efficiency
J. A. M. A., 103 (1934), 1760
Stone, Charles H., and Margolis, Julius
Granulopenia following Allonal
J. A. M. A., 103 (1934), 1933
Taylor, A. L.
The oral administration of calcium
Pharm. J., 133 (1934), 620
Underhill, S. W. F.
Clinical applications of vitamin studies
Pharm. J., 133 (1934), 591
Van Liere, Edward J., and Crisler, George
The effect of digitalis on acute cardiac dilatation produced by Anoxemia
J. Pharmacol. & Exper. Therap., 52 (1934), 408

VEGETABLE AND ANIMAL DRUGS.

Argall, C. B. K.
Japanese pyrethrum, its history, cultivation, uses and sales
Chem. & Drug., 121 (1934), 750
Freise, F. W.
Deterioration of drugs with duration of storage and mode of packing
Chem.-Ztg., 58 (1934), 853–854; through *J. Soc. Chem. Ind.*, 53 (1934), 1083B
Jaretzky, R., and Ulbrich, H.
Intraplasmatic changes in the formation of gum in the seeds of *Linum usitatissimum* and *Althæa officinalis*
Arch. Pharm., 272 (1934), 796
Kondo, H., *et al.*
Investigation of Lycoris alkaloids
J. Pharm. Soc., Japan, No. 633 (1934), 194
Kondo, Y.
Identification of drugs by means of their ash pictures
J. Pharm. Soc., Japan, No. 633 (1934), 211
Kondo, Y.
Supplement to the ash pictures of important drugs of the Japanese, German and Austrian Pharmacopœias
J. Pharm. Soc., Japan, 632 (1934), 179
Kondo, Y., and Kawamura, M.
Ash pictures of important poisonous drugs
J. Pharm. Soc., Japan, No. 633 (1934), 217
Lendner, A.
A frequent falsification of pepper
Pharm. Acta Helv., 9 (1934), 224
Lundsgaard, Einar, and Schou, Aage
Hormones and hormone preparations
Arch. Pharm. og Chem., 41 (1934), 720, 760
Munesada, T.
Pharmacognostic researches of Japanese drugs of the geranium family
J. Pharm. Soc., Japan, No. 633 (1934), 187
Noguchi, Takemi
Contribution to the knowledge of the constituents of "Sen Kyu"
J. Pharm. Soc., Japan, No. 632 (1934), 171
Oester, Y. Thomas
An investigation of Gleditschia Triacanthos (Linné)
Jour. A. Ph. A., 23 (1934), 1198

Ogata, A., and Hirano, S.
Study of the male hormone. VI, VII
J. Pharm. Soc., Japan, No. 633 (1934), 199, 227

Sattler, O. H.
On Capsicum
Pharm. Zentralh., 75 (1934), 778

Stellfeld, Carlos
Berberis laurina* as a substitute for *Hydrastis canadensis
Tribuna farm., 2 (1934), 142; through *Chem. Abstr.*, 28 (1934), 5598

Tatzel, F.
The significance of school gardens with respect to the production of inland spice and drug plants
Pharm. Post, 67 (1934), 627

ALKALOIDS AND GLUCOSIDES.

Beaune, A.
Pharmacodynamic comparison of several heart-active glucosides (ouabain, *k*-strophanthin, convallamarin, cymarin)
Bull. sci. pharmacol., 41 (1934), 590

Bermond, A.
Totaquina
Bull. sci. pharmacol., 41 (1934), 614

Chessa, G.
The stabilization of the active principles of digitalis
Arch. farmacol. sper., 57 (1934), 96; through *Chem. Abstr.*, 28 (1934), 4173

Deltour, P.
Quantitative determination of morphine in opium
Pharm. Tijdschr., 12 (1934), 169

Frangoules, J., and Basileios, A.
Investigation and determination of free acid in acid salts of quinine
Praktika, 7 (1932), 293; through *Chem. Abstr.*, 28 (1934), 5175

Greifinger, S.
Studies on the saponins of *Chenopodium ambrosiodes* L.
Wiadomosci Farm., 61 (1934), 275; through *Chem. Abstr.*, 28 (1934), 4839

Jatridos, D.
Determination of total alkaloids in cinchona bark
Praktika, 7 (1932), 281; through *Chem. Abstr.*, 28 (1934), 4835

Leoncini, G.
New color reactions for the differentiation of saligenin and phloretin from their glucosides
Boll. ist. super. agrar. Pisa, 9 (1933), 530; through *Chem. Abstr.*, 28 (1934), 4535

Manske, R. H. F.
Alkaloids of fumariaceous plants. IX. *Dicentra formosa*, Walp
Can. J. Research, 10 (1934), 521; through *Chem. Abstr.*, 28 (1934), 4537

Manske, R. H. F.
Alkaloids of fumaraceous plants. X. *Dicentra oregana* Eastwood
Can. J. Research, 10 (1934), 765; through *Chem. Abstr.*, 29 (1934), 5179

Milshtein, A., Zhukhovitzka, E., and Rosenberg, H.
Determination of quinine and antipyrine in a mixture
Farm. Zhur. (1934), 64; through *Chem. Abstr.*, 28 (1934), 5598

Offerhaus, C., and Baert, C. G.
Anesthetics with special reference to cocaine and novocaine
Pharm. Weekblad, 71 (1934), 1337, 1364

Opieńska-Blauth, J.
Determination of strophanthin in the seeds and extracts of strophanthus
Arch. Chem. Farm., 1 (1934), 29; through *Chem. Abstr.*, 28 (1934), 4538

Orekhov, A. P.
Study of alkaloids of the *Berberis heteropoda*
Khim. Farm. Prom., No. 1 (1934), 19; through *Chem. Abstr.*, 28 (1934), 5598

Regnier, J., and David, R.
On the preservation of cocaine after sterilization
Bull. sci. pharmacol., 41 (1934), 595

Sanchez, J. A.
New test for procaine and a new procedure for determining procaine and stovaine
Ann. chim. & anal. chim. appl., 16 (1934), 249; through *Chem. Abstr.*, 28 (1934), 4836

v. Klobusitzky, D.
A micro method for the determination of different strychnine salts
Biochem. Z., 270 (1934), 120; through *Chem. Abstr.*, 28 (1934), 4837

Van Esweld L,. W.
Chloretone as a preservative for epinephrine solutions
Pharm. Weekblad, 71 (1934), 131*d*

Vita, G., and Bracaloni, L.
Composition and different amorphous iodobismuthates of quinine prepared according to the method of Francois and Seguin
J. Pharm. et Chim., 20 (1934), 512

Wenusch, A., and Bilowitzki, G.
Determination of anabasine
Biochem. Z., 270 (1934), 15; through *Chem. Abstr.*, 28 (1934), 4837

Willstaedt, H.
Detection and determination of procaine
Biochem. Z., 269 (1934), 182; through *Chem. Abstr.*, 28 (1934), 4176

OILS, FATS AND WAXES.

Vanin, I. I., and Chernoyarova, A. A.
Fatty and essential oils from *Coriandrum sativum* grown in the Northern Caucasus
J. Applied Chem., 6 (1933), 922; through *Chem. Abstr.*, 28 (1934), 3833

ESSENTIAL OILS.

Brodskii, B.
Camphor from *Ocimum basilicum*
Khim. Farm. Prom., No. 1 (1934), 42; through *Chem. Abstr.*, 28 (1934), 5599
Muller, A.
Surface tension of essential oils
Helv. Chim. Acta, 17 (1934), 1135–1142; cf. *C. A.* (1932), 803; through *J. Soc. Chem. Ind.*, 53 (1934), 1117B
Scholz, G.
The determination of volatile oils in drugs
Apoth.-Ztg., 40 (1934), 1690
Schwarz, M. A.
Determination of aldehydes in essential oils
Ann. chim. applicata, 24 (1934), 352–355; through *J. Soc. Chem. Ind.*, 53 (1934), 1036B
Wasicky, R., and Gmach, E.
Macro- and micro-histochemical detection of cineol
Monatsbeilage Pharm. Presse, 5 (1934), 113

ANALYTICAL METHODS AND RESULTS.

Csipke, Z.
Evaluation of lead-containing plasters and liniments
Magyar Gyóg. Társ. Ért., 10 (1934), 292; through *Chem. Abstr.*, 28 (1934), 5177
Källström, K.
Copper determinations in iron-copper medicinals
Svensk Farm. Tid., 38 (1934), 185; through *Chem. Abstr.*, 28 (1934), 4177
Leymarie, J.
A practical procedure for the determination of moisture in pharmaceutical and food products. II. Applications
J. Pharm. et Chim., 20 (1934), 443
Nobili, G.
Activity of commercial pepsins of standard 1:100. Testing of albumin and control of peptonizing power
Boll. chim.-farm., 73 (1934), 677–680, 719–724; through *J. Soc. Chem. Ind.*, 53 (1934), 1117B
Oakley, Margarethe, and Krantz, John C., Jr.
A note on the arsenic test for reduced iron
Jour. A. Ph. A., 23 (1934), 1196
Palfray, L., Sabetay, S., and Sontag, D.
A new number applicable to aldehydes: Cannizzaro number. Application to the assay of oil of bitter almonds
Chimie & industrie (April 1934), 863; through *Chem. Abstr.*, 28 (1934), 5927
Piper, C. S.
The volumetric determination of potassium by the cobaltinitrite method
J. Soc. Chem. Ind., 53 (1934), 392T
Renaudin, J., and Renaudin, J.
On the microdeterminations by iodimetry
J. Pharm. et Chim., 20 (1934), 516
Schulek, E., and Floderer, I.
Determination of mercury in medicinal preparations
Magyar Gyóg. Társ. Ért., 10 (1934), 147–159; *Chem. Zentr.*, 1 (1934), 2459; through *J. Soc. Chem. Ind.*, 53 (1934), 1083B
Siegfried, K.
Bellier's reaction of the Swiss Pharmacopœia V
Pharm. Acta Helv., 9 (1934), 211
Thomann, J.
Determination of vioform in surgical dressings
Pharm. Acta Helv., 9 (1934), 229
Thomis, G.
Method for determining oxyhemoglobin contents of certain pharmaceuticals
Praktika, 7 (1932), 275; through *Chem. Abstr.*, 28 (1934), 4535
Weiss, L.
Evaluation of ferrum reductum by the sublimate method
Z. anal. Chem., 98 (1934), 397–402; through *J. Soc. Chem. Ind.*, 53 (1934), 1117B

INORGANIC AND PHYSICAL CHEMISTRY.

Alpers, H.
Volume relationship in magnesium oxide
Apoth.-Ztg., 49 (1934), 1643
Anon.
Determination of acidity in non-aqueous solutions
Pharm. J., 133 (1934), 595
Branch, G. E. K., and Yabroff, David L.
The anomalous strength of salicylic acid
J. Am. Chem. Soc., 56 (1934), 2568
Gabel, L. F.
Free alkali in glass
Jour. A. Ph. A., 23 (1934), 1174

Geddes, John A., and Bingham, Eugene C.
The fluidity of anisole
J. Am. Chem. Soc., 56 (1934), 2625

Malquori, G.
Stability of aqueous dispersions of lecithin
Atti congr. naz. chim. ind., 4 (1933), 752–753; *Chem. Zentr.*, 1 (1934), 2004; through *J. Soc. Chem. Ind.*, 53 (1934), 1036B

Moser, H.
Physical-chemical examination of surgical dressings. I
Pharm. Ztg., 79 (1934), 1303, 1316

Philbrick, Frederick Arthur
The association of phenol in different solvents
J. Am. Chem. Soc., 56 (1934), 2581

Remy, E.
New facts concerning physical and chemical studies of cresol soap preparations
Arch. Pharm., 272 (1934), 827

Ruemele, T.
On the knowledge of emulgators
Pharm. Zentralh., 75 (1934), 749

Savage, R. Maxwell
The absorbency of surgical cotton wool
J. Soc. Chem. Ind., 53 (1934), 379T

ORGANIC CHEMISTRY.

Feist, K., and Schultz, J.
Action of phthalic anhydride and salicylic anhydride on 2-aminopyridine
Arch. Pharm., 272 (1934), 785

Fischer, R.
On identification reactions for *l*-ascorbic acid (vitamin C)
Pharm. Ztg., 79 (1934), 1207

Gardner, John H.
The preparation of chrysophanic acid from chrysarobin
Jour. A. Ph. A., 23 (1934), 1178

Kögl, F.
On auxin
Pharm. Ztg., 79 (1934), 1272

Marion, L.
Nonbasic constituents of the leaves and roots of *Adlumia fungosa* Greene
Can. J. Research, 10 (1934), 759; through *Chem. Abstr.*, 28 (1934), 5178

Windaus, A., *et al.*
Constitution of ergosterol
Ann., 510 (1934), 248; through *J. pharm. Belg.*, 16 (1934), 1034

CLINICAL TESTS.

Chéramy, P., and Lobo, R.
Rapid method for the identification of barbiturates in blood
J. Pharm. et Chim., 20 (1934), 461

ARGENTINE CONGRESS ON MEDICAL ECONOMICS.

The first Congress on Medical Economics, organized by the Colegio Medico, a medical society of Buenos Aires, with the coöperation of similar medical societies of Argentina, was held in Buenos Aires. Important problems of collective medical practice were discussed. The members resolved to have a fixed tariff of fees, in relation to the economic conditions of patients, who were classified as "poor," "justified to have a 60 per cent reduction in the schedule," and "able to pay the whole fee assigned in the schedule." They also resolved to have the City Hospital and similar institutions as centers for free medical care. There were various general motions, such as on the preparation of a national sanitary code. The existence of sanatoriums belonging to medical coöperative and medical mutual societies were approved. The members stated that the medical profession in Argentina is overcrowded and advised the limitation of the number of students to medical schools in relation to the health demands of the country as well as the selection of candidates, according to their preparation and ethical background. The suppression of treaties of reciprocity with various countries was advised as an aim of securing practice for Argentine physicians, those graduated from Argentine schools as well as those returning home with diplomas from accredited schools in other countries.

Main entrance, Paris School of Pharmacy.

THE STABILIZATION OF SYRUP OF HYDRIODIC ACID, U. S. P. X.

BY WILLIAM J. HUSA[2] AND LYELL J. KLOTZ.

The troublesome discoloration of hydriodic acid preparations due to liberation of free iodine was overcome many years ago by use of hypophosphorous acid. The darkening of Syrup of Hydriodic Acid due to decomposition of the sugar, however, has remained as a problem up to the present time (1). The sucrose in Syrup of Hydriodic Acid is rapidly hydrolyzed into dextrose and levulose (2), (3). Haussmann (4) ascribed the discoloration to the decomposition of the levulose formed in this inversion.

In syrups of hydriodic acid containing no hypophosphorous acid, the dextrose formed on hydrolysis of sucrose tends to reduce any free iodine formed. From this point of view sucrose has sometimes been considered as a preservative in the syrup. In Syrup of Hydriodic Acid, U. S. P. X it would be erroneous to consider sucrose as a preservative because the hypophosphorous acid is fully effective in preventing the appearance of free iodine and the sucrose is the direct cause of the discoloration which occurs. Diluted Hydriodic Acid, U. S. P., will remain colorless indefinitely but as soon as sucrose is added to prepare the syrup an unstable preparation results.

From the above considerations it was thought that if Haussmann's views were correct, it should be possible to prepare a stable syrup of hydriodic acid by using hypophosphorous acid to prevent the appearance of free iodine and employing dextrose to give the preparation the properties of a syrup. Accordingly, syrups of hydriodic acid were prepared following the U. S. P. directions with the exception that the sucrose was omitted and the following sweetening agents used: (*a*) dextrose, C. P., 700 Gm. per L., (*b*) dextrose, commercial,[3] 700 Gm. per L., (*c*) Glucose, U. S. P., 435 cc. per L. The deterioration of these syrups was compared with that of a U. S. P. Syrup of Hydriodic Acid in an accelerated test consisting of storage in an oven at 50° C. in completely filled, tightly stoppered bottles. The results are shown in the following table.

As indicated in Table I, dextrose proved vastly superior to sucrose in the syrup stored at 50° C. Tests are in progress under various other conditions of storage. The C. P. dextrose gave a colorless syrup to start with while the commercial dextrose yielded a syrup of a slight yellow tint; the yellow color of the syrup prepared from U. S. P. Glucose might be considered objectionable. By use of 700 Gm. of dextrose per L., a product of excellent palatability was obtained.

According to present price quotations, a syrup prepared with the above quantity of commercial dextrose should cost about 3¢ more per liter than the present Syrup of Hydriodic Acid; a preparation containing C.P. dextrose should cost approximately 80¢ more per liter. Obviously, these slight price increases are negligible in comparison with the greater stability of the preparation.

About 35 years ago, Scoville (5) prepared samples of syrup of hydriodic acid using glucose in place of sucrose but the preparations clouded on standing. The clouding may have been due to impurities but was not observed in syrups made with any of the grades of dextrose used in the present study.

---

[1] Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

[2] Head Professor of Pharmacy, University of Florida.

[3] For this we are indebted to the Penick and Ford Co., Cedar Rapids, Iowa.

TABLE I.—DETERIORATION OF SYRUPS OF HYDRIODIC ACID CONTAINING VARIOUS SUGARS.

Syrup Containing per Liter.	Appearance of Syrups after Storage in Oven at 50° C. 0 Days.	30 Days.	60 Days.	90 Days.
450 Gm. Sucrose (U. S. P. Syrup)	Colorless	Yellow; contains ppt. which redissolves on shaking	Dark brown liquid; copious black ppt. which partially redissolves on shaking	Black solution; black ppt.
700 Gm. C. P. Dextrose	Colorless	Colorless	Colorless solution; traces of ppt. which redissolves on shaking	Pale yellow solution; traces of ppt. which redissolves on shaking
700 Gm. Commercial dextrose	Slight yellow tint	Nearly colorless	Nearly colorless; traces of a black ppt. which redissolves on shaking	Pale yellow solution; traces of a black ppt. which redissolves on shaking
435 cc. U. S. P. glucose	Yellow	Yellow	Dark yellow	Very dark yellow

SUMMARY.

It has been found that a Syrup of Hydriodic Acid of greatly increased stability can be prepared by replacing the sucrose in the official formula by dextrose. Dextrose of C.P. quality gives the best preparation although a satisfactory preparation results from the use of commercial dextrose.

REFERENCES.

(1) Husa, William J., JOUR. A. PH. A., 20 (1931), 759–762.
(2) Woltersdorff, A. H., and Richtmann, W. O., *Pharm. Archives*, 3 (1900), 81.
(3) Krantz, John C., Jr., JOUR. A. PH. A., 12 (1923), 967.
(4) Haussmann, F. W., *Am. J. Pharm.*, 72 (1900), 217.
(5) Scoville, W. L., *Drug. Circ.*, 43 (1899), 221.

SCHOOL OF PHARMACY,
UNIVERSITY OF FLORIDA,
GAINESVILLE, FLORIDA.

A STUDY OF VEHICLES FOR MEDICINES.*

BY BERNARD FANTUS, H. A. DYNIEWICZ AND J. M. DYNIEWICZ.

IX. FRUIT SYRUPS.

It may seem strange that fruit syrups, as delicious as they are and as extensively as they are employed in cooking and for the flavoring of beverages, are not used to a greater extent as vehicles for medicines. Syrup of Orange is the only U. S. P. representative of fruit syrups prescribed under its own name; and Syrup of Citric Acid, which is really an artificial lemon syrup, the only other one. In the National Formulary we have the Syrup of Raspberry.

* From the Laboratory of Pharmacology of the College of Medicine, University of Illinois.

The Syrup of Wild Cherry has quite an extensive use and might be taken to represent a sort of cherry syrup. When, however, one notes the kind of "wild cherry syrup" that is being palmed off for the official preparation, which if not actually delicious is not offensive, one is not surprised that so many people detest the taking of medicine. Some of these "wild cherry syrups" are turbid, some of them have undergone fermentation so as to be sour in addition to being bitter and highly astringent.

We understand that a new formula for syrup of wild cherry is being contemplated and it is hoped that it will be a great improvement over the present one. Nevertheless we wonder whether anyone who would have a choice between a nice syrup of cherry and the best possible Syrup of Wild Cherry would not unhesitatingly choose the cherry syrup. Thus when it comes to flavoring fountain drinks no one would think of using Syrupus Pruni Virginianæ to prepare a delicious and refreshing drink. Then why treat medicines with the less delightful flavor and taste and make it more offensive than it needs to be? We would therefore like to see the syrup of cherry introduced in the United States Pharmacopœia or the National Formulary, so as to give it a chance to compete with the Syrup of Wild Cherry for medical favor.

Possibly the reason why fruit syrups have not been introduced more extensively in official formularies is the difficulty of securing a uniformly satisfactory standardized product. Thus, for instance, the syrup of raspberry of the National Formulary V is unsatisfactory because it introduces the variable factor of fermentation, which is relied upon to destroy the pectin. Unfortunately, quite often the fermentation advances to the stage of vinegar production while the pectin is being destroyed, spoiling thereby the fine aroma of the raspberry. At other times a different form of fermentation causes the production of a musty odor which is likewise objectionable.

We therefore believe that it is very important to control the fermentation process which destroys the pectin bodies, in such a way as to have this fermentation limit itself to this effect without producing other changes.

With this in view we have experimented extensively: employing various degrees of temperature, various degrees of avoidance of exposure to air even to the extent of excluding the access of air by a layer of liquid petrolatum. We have employed taka-diastase (which was recommended for this purpose); we have tried modifying the p_H value by addition of alkali and acid, all this without entire satisfaction.

We have secured the best results by adding 0.1% of benzoic acid to the strained fruit juice and permitting the mixture to stand at room temperature until a small portion of the filtered juice remains clear when one-half its volume of alcohol is added to it.

It seems that the presence of *benzoic acid permits the activity of the pectase, while inhibiting vinegar and other bacterial fermentation.*

Objection might be raised to the presence of benzoic acid in these fruit syrups as advocated in the subjoined formulas on the ground that the use of such preservative in food products is illegal. Granted that the use of benzoic acid to be undesirable in food products that might be consumed in unlimited quantities and for an indefinite length of time, bringing the possibility of ingestion of a toxic dose,

such danger is not present in the use of a teaspoonful or even a tablespoonful of a less than 1–2000 solution of benzoic acid, several times daily for the usually limited time that medicines are taken. A great deal might be said on the subject of the joint responsibility of the prescribing physician and the dispensing pharmacist for the keeping qualities of the medicines dispensed. An investigation of the condition of medicines after they have been kept in the patients' homes for several days or longer might result in shocking revelations and in the wish that more medicines would be thrown down the sink than be forced down the unwilling throat of a struggling babe. It is well known that the keeping quality of syrups is entirely dependent upon their concentration. It is many times necessary to employ a certain amount of water to dissolve the medicinal ingredient and, unless this quantity of water be adjusted with extreme care which is usually not given it, the syrup becomes diluted to the spoiling point. The necessity of preventing this is obvious and it is respectfully submitted that the more general employment of benzoic acid or some other preservative in medicinal syrups be given more serious consideration.

That benzoic acid may introduce incompatibility is freely admitted. This is, however, no worse than the incompatibility, *e. g.*, of syrup of wild cherry with iron salts.

We therefore respectfully submit the consideration of the following three formulas for admission in the United States Pharmacopœia or the National Formulary.

SYRUPUS RUBI IDÆI.

Syrup of Raspberry.

Syr. Rub. Id.

Press the juice from fully ripe raspberries through a flannel cloth. Dissolve in the raspberry juice 0.1 per cent of benzoic acid, and let the solution stand at room temperature until a small portion of the filtered juice produces a clear solution with one-half its volume of alcohol. Then clarify the juice by straining through flannel cloth and paper if necessary, and add to each 450 cc. of the clarified juice 850 Gm. of sucrose. Dissolve the sucrose in the juice by heat on a water-bath, cool and remove the scum.

Preserve the product in well-stoppered bottles in a cool and dark place.

SYRUPUS FRAGARIÆ.

Syrup of Strawberry.

Syr. Frag.

Press the juice from fully ripe strawberries through a flannel cloth. Dissolve in the strawberry juice 0.1 per cent of benzoic acid, and let the solution stand at room temperature until a small portion of the filtered juice produces a clear solution with one-half its volume of alcohol. Then clarify the juice by straining through flannel cloth and paper if necessary, and add to each 450 cc. of the clarified juice 850 Gm. of sucrose. Dissolve the sucrose in the juice by heat on a water-bath, cool and remove the scum.

Preserve the product in well-stoppered bottles in a dark place.

SYRUPUS CERASI.

Syrup of Cherry.

Syr. Ceras.

Pit fully ripe, dark, sour cherries. Rub the cherries through a wide mesh sieve and crush kernels in a grinder. Dissolve in the mixture 0.1 per cent of benzoic acid and allow to stand for

three days at room temperature. The filtered juice should produce a clear solution with one-half its volume of alcohol. Should a turbidity form, allow the mixture to stand until a portion of the filtered juice remains clear with one-half its volume of alcohol. Press the juice through a flannel cloth and filter through paper; add to each 450 cc. of the filtered juice 850 Gm. of sucrose. Dissolve the sucrose in the juice by heat on a water-bath, cool and remove the scum.

Preserve the product in well-stoppered bottles in a dark place.

The question of policy of recognizing both raspberry and strawberry syrups might possibly be raised because of the close relation of these flavors to each other. That, however, they have rather specific disguising qualities may become, it seems to us, evident from the following two prescriptions.

In the administration of small quantities of antipyrine as in children's dosage, raspberry syrup seems to give a better disguise than most anything else we have tried. The following prescription might bear this out.

℞	Antipyrine	2.0
	Water	2.0
	Syrup of Raspberry, to make	60.0 cc.

M. and label: Teaspoonful in water every 2 hours. (For child three years old.)

℞	Sodium Citrate	15.0 Gm.
	Water	7.5 cc.
	Syrup of Strawberry, to make	60.0 cc.

M. and label: Teaspoonful in water every 2 hours.

In our opinion the same prescription with syrup of raspberry in the latter and the syrup of strawberry in the former is not quite as pleasant. Incidentally it might be mentioned that the citrates make raspberry syrup purplish; also that sodium citrate is less offensive to the palate than potassium citrate.

Syrup of cherry is an almost specific vehicle for the pleasant administration of acid as shown by the following prescription.

℞	Diluted Hydrochloric Acid	5.0 cc.
	Syrup of Cherry, to make	60.0 cc.

M. and label: Teaspoonful in $\frac{1}{2}$ wineglassful of water after meals.

The only competitor of cherry syrup is raspberry syrup which also results in a delicious combination, as is shown by the following formula.

℞	Diluted Hydrochloric Acid	5.0 cc.
	Syrup of Raspberry, to make	60.0 cc.

M. and label: Teaspoonful in $\frac{1}{2}$ wineglassful of water after meals.

The following two prescriptions might show a reason why syrup of wild cherry should be deleted in favor of syrup of cherry.

℞	Codeine Phosphate	0.25 Gm.
	Ammonium Chloride	5.00 Gm.
	Water	5.00 cc.
	Syrup of Wild Cherry, to make	60.00 cc.

and the following

℞	Codeine Phosphate	0.25 Gm.
	Ammonium Chloride	5.00 Gm.
	Water	5.00 cc.
	Syrup of Cherry, to make	60.00 cc.

It will be seen that not only does the cherry syrup yield a more pleasantly tasting dose, but it is clear, while the syrup of wild cherry is turbid from precipitation of codeine tannate.

Another comparison of interest is yielded by the following two prescriptions.

℞	Iron and Ammonium Citrate	5.0 Gm.
	Syrup of Wild Cherry, to make	60.0 cc.

and

℞	Iron and Ammonium Citrate	5.0 Gm.
	Syrup of Cherry, to make	60.0 cc.

The former is ink, the latter is merely dark, and not unpalatable; though we believe the Syrup of Cinnamon (new formula) furnishes the better vehicle.

CONCLUSIONS.

1. We advocate a change in the preparation of the syrup of raspberry consisting in the introduction of 0.1 per cent of benzoic acid in the fruit juice undergoing depectinization.

2. We respectfully submit formulas for syrup of strawberry and syrup of cherry to consideration for admission by either the United States Pharmacopœia or the National Formulary.

3. In the preparation of these other fruit syrups we also find that the presence of 0.1 per cent benzoic acid is of value in the removal of pectin while preventing vinegar formation and other fermentations.

4. The syrup of cherry becomes much more highly flavored when it is made from the cherry juice that has been permitted to stand in contact with crushed cherry stones for several days, than if made without the maceration of the kernels.

5. Syrup of raspberry seems to form a particularly useful vehicle for antipyrine in small dosage; syrup of strawberry for sodium citrate and syrup of cherry for diluted hydrochloric acid.

HOSPITAL PHARMACY PRACTICE: AN INNOVATION.*

BY J. SOLON MORDELL.[1]

In the latter part of 1925 a group of forty-five physicians and one pharmacist, members of the staff of the University Hospital and of the affiliated teaching hospitals of the College of Medicine, Syracuse University, embarked upon a program of rationalization of hospital drug therapy. This committee, representative of every branch of medical practice, and under the chairmanship of the Director of the Department of Pharmacology at the College of Medicine, was asked to investigate and to offer some organized plan to correct the existent drug situation.

Time, effort and finances were, and still are deservedly expended in improving diagnostic methods. Yet little interest has been shown in having drug treatment keep abreast of diagnostic progress. It was just such a problem which confronted this group in 1925. The condition was by no means a local one nor was it any

* Section on Practical Pharmacy and Dispensing, A. PH. A., Washington, D. C., meeting, 1934.

[1] Pharmacist, Syracuse University Hospital of the Good Shepherd, Syracuse, New York.

more serious than in other institutions. In many respects the movement was pioneer in nature and had little assistance in the way of precedent.

The efforts of this committee were consummated by the publication of the *Interns Handbook*.[1] This book, which includes a description of emergency medical and surgical procedures, presents as one of its important achievements a drug list which exhibits drugs of proved therapeutic value and those which are felt to be the most efficient of their respective groups. The list is unencumbered by drugs which duplicate one another's action. Selections were made from the *United States Pharmacopœia*, the *National Formulary, New and Nonofficial Remedies* and *Useful Drugs*. Each item gained its place after it had been considered meticulously from every standpoint. Whim and custom were brushed aside and replaced by a scientific, common-sense attitude. The list is outstanding because of the scarcity of so-called "specialties." Preparations of official drugs under fanciful names are absent, as are items whose formulas are secret. Digitalis, ergot, cresol solution, liquid petrolatum and a host of others are deemed efficient *per se*. No sympathy is extended to embellishments of these items and the exorbitant price premiums entailed. In the rare instances where specialties were approved for admission, it was for the reason that they possess unique value not available in other preparations. In no case were specialties considered unless accepted by the Council on Pharmacy and Chemistry of the American Medical Association; this, among other considerations, implies that formulas and standards are not secret. Similarly, wherever several manufacturers are bidding for the same item, preference is given to the product approved by the aforementioned Council.

The drugs are not grouped and classified according to therapeutic use, but listed alphabetically, by Latin title. The object was to induce a feeling of independence on the part of the prescriber in so far as application of the various drugs is concerned. It was felt that to suggest therapeutic uses would put prescribing on a cataloging basis and would discourage individual initiative in this respect.

The list of approved drugs included as a part of the material presented in the *Interns Handbook*, once officially adopted, laid the foundation for a reorganization of the entire system pertaining to the issuing of medicaments. It was not until 1929—four years after the establishment of the committee—that the *Handbook* was published and sold throughout the world. This wide distribution was possible because the material presented was not individualized to the group here but was made applicable for most hospitals. At this writing, the book is in process of revision.

During the four years of work on the original project, and for three years thereafter, the ground was being carefully prepared for reconstruction in the Pharmacy and throughout the hospital. After having secured the coöperation and sympathy of the heads of the various services, the work had to be done cautiously. A radical transplanting would have been disastrous to the whole plan. Each step had to be studied most carefully before it was put into operation. It should be noted that the guiding hand in all this work was that of a specialist in pharmacology, whose knowledge of drug markets as well as drugs is such as to make him constantly aware of the fads in medicine and to prompt him to assume a very critical attitude in all matters pertaining to the uses of drugs. Coöperation between a

[1] J. B. Lippincott Company, Philadelphia, Pa.

physician of this type, experienced in therapeutic problems, and a pharmacist possessing the necessary training and professional ideals, is prerequisite to the success of an undertaking of this nature.

Finally, in the summer of 1932 the situation was ripe enough to permit a general housecleaning in the Pharmacy and in the drug cabinets throughout the hospital. This work involved not only the discarding of all undesirable drugs and drug preparations, but a careful revision of buying methods. By October 1932, the eight hundred drugs previously inventoried in the Pharmacy were reduced in number by over five hundred, leaving an inventory of approved items of less than three hundred. Comparing this with the inventory of one hospital which, in reply to a questionnaire by the chairman of the committee, reported seven hundred, while other large modern hospitals reported as high as seven thousand, and eight thousand,[1] one gets a picture of the inroads which the drug situation, if uncontrolled, may make in the hospital budget. There is an analogous condition in retail pharmacies. We can find sections of shelf space in most retail establishments, which have four or five, or even more items identical in composition. The pharmacist, unfortunately, does not entirely control the situation. He must maintain a stock which will prepare him to meet all demands.

The picture in the hospital here is different. Under proper guidance, useless waste is eliminated. The following is a list of regulations formulated to cover pharmacy service in this institution:

"(1) The Pharmacy is placed under the supervision and direction of the Department of Pharmacology, in so far as the supply and standardization of drugs for use on ward cases is concerned.

"(2) This implies that the Director, together with the Pharmacy Committee and the Pharmacist, possesses or is able to secure special information concerning drugs, not easily accessible to others of the hospital organization, and will undertake to supply such information as occasion arises. Decisions of the Director, in conjunction with the Pharmacy Committee and the Director of the Service involved, on such matters as quality and integrity of drugs, are to be on the same basis as those of the Heads of other clinical laboratories, and are to be overridden only in emergency.

"(3) Additions and deletions of drug stock, and changes in forms of drugs, shall be effected only after conferring with the Directors of the Services involved, who may also recommend changes including the addition of new remedies. Advice and counsel may be obtained by them from the Department of Pharmacology whenever questions of the relative merits of these new remedies shall arise. However, when these newer preparations are used as a part of a controlled clinical investigation, the Directors of Medicine and Surgery shall be responsible for such investigation and shall determine whether they shall be used, the Director of the Pharmacy merely acting in an advisory capacity."

The above regulations are directly applicable in hospitals affiliated with a college of medicine, but the details may be adjusted to suit conditions in hospitals which do not have this connection.

Only those drugs which appear on the approved list may be prescribed for ward patients. The hospital ruling with regard to private patients is that drugs not regularly stocked are purchased especially, in the least possible quantity. The patient is charged with this quantity, even though it may materially exceed the

[1] "The Doctor and the Hospital Pharmacy," M. S. Dooley, M.D., director of Pharmacy and chairman of Pharmacy Committee, University Hospital, and *Interns Handbook* Committee; *Bull. Am. Hosp. Assoc.*, January 1931.

amount actually needed. In many such cases visiting physicians have inquired as to the corresponding item regularly stocked and approved, and have ordered it. This has usually served to reduce the patient's bill considerably with no sacrifice of therapeutic efficiency.

Advice and information are available at the Pharmacy. Here, by virtue of contact with so many physicians, the hospital pharmacist has a splendid opportunity to demonstrate to them the proper uses of vehicles and flavors; to help them construct an efficient and palatable prescription. Of course, all questions out of the pharmacist's scope are submitted to the pharmacologist.

The following procedure is used in issuing drugs: Each division (fourteen in number) sends a partitioned wire basket to the Pharmacy in the morning. Empty stock containers are included in these baskets for refilling according to an order book which, after having been checked by the nurse in charge of the division, is counterchecked and signed by a supervisor of nursing. Special orders originating during the night, for prescriptions or items not regularly stocked, are also listed in this order book. Orders presented during the day are made out on separate requisition blanks, also signed by the nurse in charge and countersigned by a supervisor of nursing. These orders have, in addition to the desired item or items, a notation of the dosage to be given, which dosage is checked by the pharmacist. In instances where patients are leaving the hospital, a notation to that effect is made. The pharmacist, in such cases, places only the directions on the label, instead of the ingredients, as is ordinarily done with containers issued in the hospital.

As part of the reorganization activities, a radical change was made in the equipment for handling the various medicaments. Uniform screw-capped, green-glass vials are used for tablets, capsules and pills, instead of pasteboard boxes. Liquids are supplied in bottles of the ebony screw-cap type. All vials and bottles bear typewritten labels coated with a suitable label varnish. These containers are used for items which constitute the regular stock supply on each division. Since special orders are used only during the stay of the patient using them, they are issued in pill boxes or in corked bottles.

The official English title of the Pharmacopœia or National Formulary is used on all labels. If in neither text, an approved title is designated by the Pharmacy committee. This eliminates misunderstandings which arise when all sorts of common names and synonyms are used. The English, rather than the Latin title, is used for the reason that the nurses receive no special instruction in the Latin of pharmacy. Prominence is given throughout to the metric system.

Another step in the reorganization consisted in equipping all divisions uniformly. Since the hospital includes a school of nursing which rotates student nurses throughout the various hospital divisions, it contributes greatly to efficiency if the nurse does not have to be confronted with a different drug arrangement with each change she makes. The same applies to private duty nurses, since a change of patient may mean a change in location in the hospital. In addition to uniform arrangement and lay-out, a stock list is posted on each division. This list is valuable in several ways. *First*, it is a guide whereby each division may intelligently replenish its stock of drug supplies; *second*, it guides the new student nurse who is acquainting herself with the equipment of the particular ward concerned; *third*,

it controls any overloading of drug supplies throughout the hospital; and *fourth*—a matter of extreme importance—it serves as a control for the pharmacist, obviating waste in supplying the hospital, and enabling him to prepare his own stock intelligently.

The most recent improvement effected has been the establishment of a central supply room in conjunction with the Pharmacy. This coördination does not usually exist in other hospitals. Under the new arrangement, the preparation and sterilization of solutions for parenteral use (such as Physiological Sodium Chloride and Ringer's), as well as the sterile dressings and various sterile trays (hypodermoclysis, intravenous, thoracentesis, paracentesis, etc.), are all carried out in this specially equipped room. Previously these operations had been performed in another division of the hospital, which division combines several different activities. The principal advantages sought by the change were, *first*, that of having the solutions prepared and sterilized under the supervision of the pharmacist, and *second*, that the unit would be specialized for the above-mentioned functions instead of being part of a conglomerate department. To effect this change, it was necessary to break through one wall of the Pharmacy into a room formerly used for excess stock of another department. As a result, the pharmacist is able to have constant surveillance of operations. The actual work is handled by a capable graduate nurse who has had special instruction and experience in this branch, while the pharmacist checks all operations and acts in a consulting capacity.

No little advantage has accrued to the hospital's financial situation as a result of the work done in the pharmaceutical end. Without sacrificing quality and efficiency, the replacement of costly specialties by their corresponding official drugs wherever possible, and the elimination of questionable patent medicines and nostrums has meant savings which, during the first year of operation of the new set-up, ran into four figures. It is quite certain that the second year's operations will reveal a considerably greater saving. It is important to note that the original primary aim was solely to rationalize drug therapy. The marked financial advantages which attend such a plan are, therefore, significant and satisfying.

Through the efforts of the AMERICAN PHARMACEUTICAL ASSOCIATION, the Council on Medical Education and Hospitals of the American Medical Association has initiated a move in the right direction with regard to hospital pharmacies.

As described in the April 1934, JOURNAL A. PH. A., this Council has included in its "Essentials of a Registered Hospital" the one requiring that "the handling of drugs should be adequately supervised and should comply with state laws." The next step might well be that of establishing minimum standards in hospital pharmacies with regard to the nature of drugs handled. Much has been accomplished by the various medical groups concerned, with regard to standards for the operating room, the X-ray division, Physiotherapy, etc. In coördination with the AMERICAN PHARMACEUTICAL ASSOCIATION, the American Medical Association can do much to raise hospital pharmacies to the standards it has so admirably reached in the other departments of the hospital.

HISTORY IN THE DRUG STORE.*

BY FRED B. KILMER.[1]

Only in a limited way has history yet entered the drug store, and reached the man behind the counter. Eminent authorities from this ASSOCIATION have made highly important contributions to the history of pharmacy. For the most part, the pages upon which their records appear lie unopened and unread. The drug store man is not history-conscious.

Possibly, we have too much history. The progress of the world, the advance of science, of pharmacy and of the art of printing have evolved such a vast collection of historical material that the ordinary man finds life too short to even glance at them.

At times the druggist adopts Henry Ford's dictum that "history is bunk." He lets the past bury the past. With him events begin with the day he was graduated from college, got married or bought his first store. With many astute men nothing back of the World War, the depression or the NRA counts. This is a very human point of view for the man of to-day.

Few pharmacists have come to realize the uses and value of history. History is filled with lessons wherein we may learn to profit by the example and teaching of those who have gone before us in a world and a society not unlike the one in which we live. A knowledge and understanding of the realities of the history of pharmacy, and of the sale and dispensing of drugs, would help us to avoid many of the perplexities and catastrophes which now afflict us. The real lessons of history can be turned into dollars.

Rarely does the pharmacist reach to the delights of history. History helps us to know what our ancestors did—their troubles, their faults and their successes. It presents a story, a moving picture of life. History presents a marvelous play, with interludes, by-plays, changes of tone, changes of scene. One can find in history things that are romantic, picturesque, artistic and beautiful.

WRITTEN HISTORY.

There exists an abundance of written history. The shelves of our libraries are loaded with historical volumes. The pages of our magazines are crowded with historical essays.

Even with this array, the fact seems to be that history is not yet a popular subject. Historical volumes cannot be counted among the "best sellers." Pharmaceutical history has not yet penetrated behind the drug store counter.

In part, this condition may be due to the mode and manner of its presentation. Right here the historically minded reader may well say to the writer: "Who are you to tell us how we should write history?" Well, the author of this essay, with all humbleness, acknowledges that he is only a smatterer in history. He is not a historian. As a most humble student he, with due deference to the many eminent historians, offers the suggestions of a rather awkward beginner.

Much of our written history of pharmacy has been put together by able professional historians. Much of it has been written by the historical scholar. Facts,

* Section on Historical Pharmacy, Washington meeting, 1934.

[1] Deceased.

dates, footnotes, references and proofs abound in the pages. Often the author seeks to fortify himself against the criticisms of other historians. Readability and attractiveness are sacrificed.

Facts and dates, while highly important, taken alone do not make history. When the historian of the pick and shovel, the paleontologist, finds a skull or the bones of a jaw of a man who lived centuries ago, he must make the dry bones live. From the rocks under which his "find" was buried he determines the era in which his man lived. Hypothetically, he supplies the missing parts with plaster and putty. He lays on tints, and lo! we have a man who lived two thousand score years ago.

To record the history of pharmacy in any age we must take note of political and social events, the advancement of science, changes of policy, changes in taste, dress, ways of living, comforts, books, plays, popular songs and many things which make up and control human life and activities. In the midst of these, pharmacy and the drug store have lived and moved. History cannot be divorced from life.

To fulfil its mission, written history must be read. The reader must "read, mark and inwardly digest," and finally apply its lessons to his life and work. We may well believe that the history of pharmacy can be presented in such a way that it will reach into the drug store, and that the man behind the counter will live and move in its elevating air. The craftsmanship may weil be left to our most capable producers of pharmaceutical history.

The AMERICAN PHARMACEUTICAL ASSOCIATION, through its museum and repository, will become a notable center for pharmaceutical history. Unfortunately, our pharmaceutical and trade associations have done but little along historical lines. A survey revealed that certain associations did not have on file complete copies of their own proceedings. Very meager were instances where there was an attempt to preserve historical data as to their organization. Associated effort in pharmacy contains an important record of the progress of the art. It is well worthy of preservation and use.

Pharmaceutical manufacturers, in a limited way, have found it wise to give attention to the history of their calling and their own organization. Some of them have installed a historical department or museum wherein are collected records, specimens of early productions, advertising and other data. Collections of this character have proved to be of service in the education of salesmen, detail men and others, as to the historical background of the institution. Notable have been the collections pertaining to general historical pharmacy acquired by certain manufacturers.

The retail druggist can, through history, draw patronage, gain reputation and increase his prestige. The use of historical elements will give a new and a different twist to drug store publicity. Above all other practitioners of the art of pharmacy, the retail druggist can turn history into cash. An economical method is through historical displays.

Drug store historical exhibits may consist of window displays, which may be moved to the interior of the store, and within the store moved from one point to another, forming a continuous show. A well-planned historical exhibit will hold attention from two weeks to a month. From one to twenty historical exhibits can

be given annualiy. Through changes, historical exhibits can be repeated from year to year.

The druggist may properly use his exhibits as an advertising medium. Physicians, nurses, professional men, prominent citizens and college and high school classes are worthy of special invitations. The local papers will be glad to give special write-ups of the show.

Subjects with which to form an historical display in the drug store are abundant. The history of the art of pharmacy may be shown by pictures clipped from magazines and books, through old-time implements and apparatus, side by side with modern types. The map issued by the National Wholesale Druggists' Association, showing pictures of colleges of pharmacy, may form a background, giving the present-day status of pharmaceutical education. College diplomas, certificates of registration and association memberships of the store owner and clerks will show that the personnel of the store stands high professionally. One druggist excited curiosity by having his clerks, during his exhibits, wear the time-honored green baize apron.

The drug store historical exhibit may well begin with a history of the druggist's own store, and his own town. Dependent upon the age of the store and the town, abundant material may be found. Pictures of the town as it was and as it is. Methods of transportation from the day of the ox-cart on to the auto and the aeroplane. Old churches, old schools, hospitals, streets and dwelling houses contrasted with the new, including the druggist's own store as it was and as it is. To these may be added pictures of old-time citizens, old doctors and their prescriptions, and notable events of the past.

Included in a series of exhibits pictures pertaining to the history of medicine might be utilized. Here an abundance of material is available.

The subjects for an historical display are extensive. A few examples may be noted: Old-time animal remedies in contrast to modern animal serums. Ancient bolus and uncoated pills as against modern pills, capsules and tablets. Crude drugs of the past by the side of present-day alkaloids, concentrations and synthetic compounds. Charms formerly used as cures in conjunction with to-day's rational remedies.

A most creditable display was shown in the *Druggists Circular*, for March 1934, which by means of cards and objects exhibited four thousand years of pharmacy and medicine, beginning with the time of the Egyptians, and concluding with the twentieth century.

Another recent exhibit was along the lines of the history of surgery. The art of surgery has been completely revolutionized within fifty years. While the use of ether is of the nineteenth century, local anesthetics have come into vogue.

A show in the history of surgery, which made everybody stop, consisted of the showing of a frock coat, used up to the late nineties as a surgeon's operating uniform, side by side with the outfit of the modern operator's cap, face mask, white gown and rubber gloves.

For history to reach into the drug store, it would seem that the beginning should be made in the college of pharmacy. A knowledge of the history of the arts to which he is to devote his life should be an inspiration and incentive to the stu-

dent to move forward. Once imbued with this knowledge, he would no doubt carry it to those with whom he may be associated.

In the preparation of this paper, correspondence was had with the deans of some of our colleges of pharmacy as to the place of the history of pharmacy in their colleges. Briefly stated, the situation would be somewhat as follows:

A moderate percentage of the colleges of pharmacy possesses a historical museum; likewise, a collection of data, documents, etc., pertaining to their own institution. A number of the colleges have in their libraries volumes relating to the history of medicine, pharmacy and allied arts. Courses covering the history of pharmacy are given in a goodly number of the colleges. In some of them it is short, covering only two hours in the three or four years' course. However, in some colleges the course is quite extended and complete. Encouragingly, there is reported a moderate interest by students in history as it pertains to pharmacy.

Many of the deans kindly made suggestions as to methods whereby the interest of students and graduates in pharmaceutical history could be increased. These suggestions will be made the subject of a separate paper.

This paper is primarily suggestive. An attempt is made to show that history, especially the history of pharmacy, has not yet reached into the drug store;

That for the great majority of druggists and their clerks, the subject of history has little or no interest;

That while able historical writers have produced much valuable historical data, it has not yet created an historical atmosphere for the rank and file of pharmacists;

That here is an opportunity for our associations to further stimulate interest in historical subjects;

That the practicing pharmacist—the druggist—can, through historical displays, promote an interest in the history of medicine and pharmacy to his own advantage.

HISTORY OF THE CALCIUM LACTOPHOSPHATE PREPARATIONS.[1]

BY WILLIAM J. HUSA[2] AND A. P. McLEAN.

Calcium lactophosphate came into use as the result of the suggestion of an European physician, Dr. L. Dusart, who, in 1869, recommended the use of calcium phosphate dissolved in lactic acid (1). In 1871, William Neergaard (2), a pharmacist of New York City, upon the request of Dr. B. W. McCready, prepared a syrup of calcium lactophosphate by dissolving freshly precipitated calcium phosphate in a diluted lactic acid, and adding water, orange flower water and sugar. This is the oldest record we have found of the use of calcium lactophosphate in this country. It was the spark which was followed by a blaze of tremendous popularity.

Because of the demands of physicians for numerous combinations of calcium lactophosphate, preparations other than the syrup came into use. Some of these, such as the elixir, the syrup with iron, and the salt, received official recognition, and there were a number of others, not so recognized, including the solution, the wine, and the emulsion with cod liver oil.

---

[1] Section on Historical Pharmacy, A. PH. A., Washington meeting, 1934.

[2] Head Professor of Pharmacy, University of Florida.

After the article published by Neergaard in 1871, giving a formula for a syrup, a number of somewhat similar reports appeared in other journals. These were written in the main by pharmacists, who suggested their own preferred formulas, or some slight modifications of formulas, which to them seemed to give better or more stable preparations. In the syrup as well as the other preparations the principal difficulty encountered was the formation of a precipitate. Little attention was paid to the cause or nature of the precipitate, but efforts were made to delay or decrease the precipitation by changing the ingredients or varying the amounts. By 1880 the syrup of calcium lactophosphate had come into such wide use that it was recognized in the U. S. P. VI, and was also official in the U. S. P. VII, VIII and IX but was dropped by the U. S. P. X and taken up by the N. F. V.

The first record found of Elixir of Calcium Lactophosphate was its recognition by the N. F. I. It was also official in the N. F. II, III, IV and V. Syrup of Calcium Lactophosphate and Iron has been similarly recognized by each edition of the N. F.

For some years there was a difference of opinion regarding the chemical nature of calcium lactophosphate. Rother (3) considered it to be a double salt while Sambuc (4) stated that the salt was merely a mixture of calcium lactate and calcium phosphate. When calcium lactophosphate in the form of the salt was recognized by the N. F. IV, it was defined as "A mixture in variable proportions of calcium lactate, calcium acid lactate and calcium acid phosphate."

Among the unofficial preparations of calcium lactophosphate, the wine seems to have enjoyed little popularity in comparison with the others, perhaps because the alcohol of the wine made the preparation undesirable for children and it was for children that the preparations were mostly used. The solution of the salt likewise did not find extensive use

The emulsion of cod liver oil with calcium lactophosphate enjoyed very wide popularity as an unofficial preparation. The earliest formula found was that of W. G. Moffit (5) published in 1873. Other formulas were proposed and commercial emulsions were put on the market by some of the manufacturers. The emulsion was criticized on pharmaceutical grounds by Polk (6), who also made the following statement:

> "The cry of 'Eureka' which has ascended so loudly over the new hobby, lactophosphate of lime and cod liver oil, it seems has almost led the enthusiastic members of the medical profession to hope that the great specific for all the ills to which flesh is heir had at last been found. The long high-sounding name ..... leads us to regard it with respect and confidence ..... The errors of the combination, outside of the quackery into which it has been run, however, immediately concerns us ....."

The emulsion was popular for about five years and after that no further record could be found in the literature.

Polk's denunciation of emulsion of cod liver oil with calcium lactophosphate appears unjustified in view of later developments. It is now accepted by medical authorities that rickets may be due to a dietary deficiency in any one of three things, *i. e.*, calcium, phosphorus or vitamin D. The emulsion of cod liver oil with calcium lactophosphate contained all three of these substances needed for proper development of bones, hence it seems unfortunate that the preparation did not remain popular. At the time the emulsion was introduced, vitamins were yet to

remain undreamed of for four decades. The emulsion thus suffered the fate of other innovations which are too far ahead of their time. In passing it is of interest to note that at about the same time that the emulsion fell into disuse, a physician made extensive reports on the value of sunshine in rickets and other diseases but he likewise was too far ahead of this era of irradiated food, irradiated drugs and irradiated human beings.

REFERENCES

(1) Dusart, Dr. L., *Archives Generales de Médecine*, December 1869, January and February 1870, cited by reference (2).
(2) Neergaard, William, *Am. J. Pharmacy*, 43 (1871), 243–244.
(3) Rother, R., *Ibid.*, 55 (1883), 607–610.
(4) Sambuc, M., *Arch. pharm.* (June 1887); through PROC. A. PH. A., 35 (1887), 286.
(5) Moffit, William G., *Am. J. Pharm.*, 45 (1873), 154–157.
(6) Polk, C. G., *Ibid.*, 46 (1874), 102.

SCHOOL OF PHARMACY,
UNIVERSITY OF FLORIDA,
GAINESVILLE, FLORIDA.

Pharmacists at the 50th Anniversary Celebration of the Institute of Pharmacy, University of Liege.

Front row (left to right)—Professors Goubau (Ghent), Herrissey (Paris), Van der Wielen (Amsterdam), Schoofs (Liege), Van Itallie (Leiden), Perrot (Paris), de Graaf (Utrecht). Back, from left—Prof. Sternon (Liege), Prof. Vivario (Liege), Mr. H. N. Linstead (Britain), Prof. Van Os (Gröningen); Prof. Stainier, Dr. Hofman (The Hague), Col. Thomann (Switzerland), Prof. Faurholt (Brussels), Prof. Ohlsson, Prof. Wattiez (Brussels), Prof. Goris, Prof. Van de Velde, Prof. Castille (Louvain), Prof. Penau, Dr. Jermstad (Oslo), Prof. Van de Vorst.—*Pharmaceutical Journal*, Dec. 22, 1934. Please see JOURNAL A. PH. A., December 1934, page 1243—note type error "Normal Arsenic."

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

"The attitude of the American Association of Colleges of Pharmacy on the question of food and drug legislation was well expressed last year when Dean DuMez and the Chairman of the Executive Committee appeared before the Senate Committee considering Senate Bill 2800 and again when the Association met in annual convention and passed a resolution indicating that the Association favored proper food, drug and cosmetic legislation. Our Association has a strategic position because its membership is not financially interested in food, drugs and cosmetics, nor actually involved in the administration of laws governing the distribution of food, drugs and cosmetics and therefore we can take a totally disinterested view of these matters. As citizens we must be vitally interested in the protection of public health and that is especially true in the case of teachers of pharmacy, since we are training young men and young women to go into one of the public health professions. The following statement by President Little of the Association has the approval of the Executive Committee and it sets forth the position we believe the Association should assume."
—C. B. JORDAN, *Editor*.

FOOD AND DRUG LEGISLATION.

One of the most important questions claiming the attention of pharmaceutical educators this winter is the problem of a sane, adequate, revision of the Pure Food and Drug Act.

The activity of the American Association of Colleges of Pharmacy in helping to promote such a revision needs no justification. We would oppose the idea that the function of colleges of pharmacy is to concern themselves solely with problems of education. That, to be sure, is their major activity, but by no means their sole responsibility. Pharmacy can hope to achieve its maximum accomplishment, only by having all of its various branches stand ready and eager to put their shoulders to the wheel and to play their full part in every possible contact.

It is in this spirit and with this hope that the American Association of Colleges of Pharmacy approaches the problem of food and drug legislation.

One of the most pathetic persons with whom we come in contact is the individual who fails to have definite, concrete opinions concerning important problems which are presented to him in his own or closely related fields. We might place second on this list of pathos, the individual who displays inadequate appreciation and respect for the other fellow's opinion. There is no reason whatsoever why tolerance and definiteness of opinion should not go hand in hand.

Pharmacy has become an exceedingly broad field, with many different interests and activities represented. It is but natural that many of these interests should possess somewhat different ideas as to what constitutes a sane, effective revision of the Pure Food and Drug Act. It is also equally certain that all these various branches of pharmacy have much in common. It is on this common ground that we should marshal and unify our forces and through concerted, efficient action accomplish much in the field of food and drug legislation.

Is not the best procedure to first search out all the various viewpoints and objectives which the different branches of pharmacy have in common? Let none escape us. The greater this pool of common interests, the stronger will be our cohesion and solidarity and hence the greater our accomplishment.

Should the time come, and we sincerely hope that it may not, when certain groups must draw apart to prepare separate bills, let us part with the finest appreciation of the other fellow's viewpoint. Let us part in a spirit of friendship and cordiality, with each group definitely pledged to carry into the product of its individual efforts the very maximum of that which has been commonly agreed upon.

From this point on, those purposes and recommendations which are most meritorious and most completely in accord with public health and welfare should prevail.

If we keep this fundamental objective of public health ever before us as our goal, no really profound differences are likely to develop and a sane, progressive and generally desirable revision of the existing law should not be difficult of attainment.

At the annual meeting of the American Association of Colleges of Pharmacy held at Washington last May, the Association went unanimously on record as favoring Senate Bill No. 2800 or a measure of greater merit. That, I believe, represents the attitude of the Association at the present time.

As president of the American Association of Colleges of Pharmacy, I have appointed a special committee, consisting of Dean Andrew G. DuMez, Dean Wortley F. Rudd and Dean Charles B. Jordan, Chairman, to represent the Association as our Committee on Food and Drug Legislation. I have also appointed an auxiliary committee consisting of one or more representatives in each state, to coöperate with the smaller committee as opportunity to do so presents itself. This larger committee will later receive specific directions and suggestions as to ways and means of assisting with our legislative program. In the meantime, we are organized and ready for action.

At a meeting of the National Drug Trade Conference held at Washington, D. C., on Wednesday, December 5th, Dean DuMez again set forth the position taken by the American Association of Colleges of Pharmacy with respect to proposed food and drug legislation by a statement of the more important provisions which the Association maintains should be incorporated in any new legislation. These provisions are as follows:

1. A new definition of the word "drug" to bring within the purview of the law certain substances (glandular products) and certain devices not always marketed as therapeutic agents in a strict interpretation of the meaning of that term, but which, when used as directed, may produce marked alterations in the tissues of the body or the functioning of its organs, as for example, devices for increasing stature, devices for developing the bust, devices for stimulating the activity of the prostate gland, nose straighteners, electric belts, etc.

2. Provisions for bringing cosmetics within the scope of the law.

3. Provisions which will make it obligatory for a manufacturer or distributor who puts up drugs or medicines in packages for sale to the public to state on the label the name, or names, of the substance, or substances, upon which the therapeutic or palliative claims for said drugs or medicines are made, and the quantity, or quantities contained in a single dose.

4. Provisions for the control of the manufacture, sale and distribution of poisonous, habit-forming or deleterious drugs, or medicines containing any of said classes of drugs, to whatever extent is necessary to give the public adequate protection against the harm which may result from the indiscriminate sale of drugs and medicines of this character.

5. Provisions for prohibiting the advertisement on the label, package, and/or by any other means of any drug or medicine as a treatment or cure for any of the following diseases: albuminuria, appendicitis, arteriosclerosis, septicemia, cancer, carbuncle, cataract, cholecystitis, diabetes, diphtheria, dropsy, encephalitis, epilepsy, erysipelas, gall-stones, heart diseases, high blood pressure, mastoiditis, measles, meningitis, mumps, nephritis, otitis media, paralysis, pneu-

monia, poliomyelitis, prostate gland disorders, pyelitis, scarlet fever, sexual impotence, small pox, tuberculosis, tumors, typhoid fever, uremia and venereal diseases.

6. Provisions for restricting the advertisement of any drug or medicine, regardless of the medium used for exhibiting or disseminating such advertisement, to the truthful statement of facts with respect to any or all claims made for the palliative or curative properties, and/or its value in the treatment of disease.

This stand represents the opinion of the Executive Committee of the A. A. C. P. and a very high percentage of the individual members of the Association as well.

I sincerely hope that our members will actively concern themselves with food and drug legislation during the coming session of Congress and that all controversial questions which may arise will always be settled on a basis of public health and welfare.

As long as we keep public health as our platform, the very foundation of all our activities, we cannot seriously err. If we relinquish this guiding motive, we may wander far astray.—ERNEST LITTLE, *President*, American Association of Colleges of Pharmacy.

GENERAL REGULATIONS, SERIES 4, FEDERAL ALCOHOL CONTROL ADMINISTRATION.

A proposed regulation, under consideration by the Federal Alcohol Control Administration, would have placed pharmacists in *the class of dealers in beverage alcohol;* it would have increased the cost of their supply of ethyl alcohol and required them to take out Federal and, perhaps, local licenses; thus adding further costs to the pharmacists' burdens, without giving additional protection to the government service. The points are, the proposed ruling, if it had been adopted, would have increased the cost of alcohol to the pharmacist, because he would have had to buy in gallon bottles, paying a higher price and also be subject to the licenses referred to, and be placed in the class of *dealers in beverage alcohol.*

THE AMERICAN PHARMACEUTICAL ASSOCIATION asked the privilege of being heard and impressed that practicing pharmacists should be enabled to freely secure alcohol for medicinal preparations at lowest cost, not only in their own interest but also in the interest of those in need of medicine. This appeal was influential in promoting the regulation to which reference is made and issued January 22 by the Federal Control Administration. Because these regulations are informative relative to general definitions and terms, every pharmacist should secure copies from the station of the Department nearest to them. Two paragraphs are quoted:

"In issuing these Regulations the Administration has provided that alcohol and other distilled spirits in containers of a capacity of one gallon or less shall be deemed to be for non-industrial use. The effect of this provision will be to require all wholesale druggists, industrial alcohol plants and others, who do not hold Federal Alcohol Control Administration permits, to supply the needs of drug stores, hospitals, pharmaceutical manufacturers and other industrial alcohol users in containers having a capacity of more than one gallon."

"Heretofore the Regulations of the Treasury Department, which require that beverage distilled spirits for sale at retail be placed in glass liquor bottles, have not been applicable to alcohol. The Treasury Department, however, acting in coöperation with the Administration, and desiring that all spirits for beverage use be definitely distinguishable from spirits intended for industrial purposes, is amending its Bottle Regulations so as to require that on and after April 15, 1935, all distilled spirits, including alcohol, if marketed in containers of a capacity of one gallon or less, shall be placed in glass liquor bottles manufactured under Treasury permit and having blown therein the indicia required by Treasury regulations."

The AMERICAN PHARMACEUTICAL ASSOCIATION always seeks to be of service to pharmacy and pharmacists.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1934–1935.

Office of the Secretary, 2215 Constitution Avenue, Washington, D. C.

LETTER NO. 9.

December 20, 1934.

To the Members of the Council:

48. Minutes of the Meeting of the Executive Committee. Motion No. 2 (Council Letter No. 2, page 846) has been carried. President Fischelis requests that he be recorded as voting "No" on this motion.

49. Committee on the Proposed Council on Pharmaceutical Practice. Chairman Cook has submitted the following report for this Committee with the statement that the report has the endorsement of all members of the Committee who were present at the meeting on August 18th. Chairman Cook expressed the belief that although the actual carrying out of the plan will be dependent upon some scheme of finance which it is hoped can be developed, it will be an advantage to have the plan presented in full and discussed so that it can be better understood.

REPORT TO THE A. PH. A. COUNCIL ON THE SUGGESTION TO ESTABLISH "A NATIONAL COUNCIL ON PHARMACEUTICAL PRACTICE" AS AN ACTIVITY OF THE A. PH. A.

The proposal was presented at the Second General Session of the AMERICAN PHARMACEUTICAL ASSOCIATION at its 1934 meeting (see the JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION, 1934, page 601) and was also brought before the Council and referred to a special Committee with a recommendation for action.

Considerable correspondence ensued and a meeting of the Committee was called in Washington for August 18, 1934. The following were present: Messrs. Arny, Cook, Fischelis, Jordan, Kelly, Spease and Swain. Messrs. Gaw and Gathercoal were unable to be present although Professor Gathercoal sent a communication outlining his views.

The discussion was general and included many of the problems which enter into to-day's pharmaceutical practice in this Country.

It was believed especially important to avoid creating an impression that the AMERICAN PHARMACEUTICAL ASSOCIATION was discriminating between pharmacists, since its sole object was to uplift every branch of pharmacy.

Every practicing pharmacist would be invited to participate, and, while not all would care to do so, the reasonable and proper specifications intended, should permit any properly trained and equipped pharmacist to register.

The following recommendations were approved for the consideration of the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION.

1. That there be recommended to the Council the establishment of a "Council on Pharmaceutical Practice" to be conducted under the auspices of the AMERICAN PHARMACEUTICAL ASSOCIATION.

2. In the recommendation to the AMERICAN PHARMACEUTICAL ASSOCIATION Council it is to be indicated that the objects of this group are to promote improvement in pharmaceutical practice by the following activities:

(*a*) The assembling of information and facts from all available sources concerning the efficient practice of Pharmacy in

(1) Retail Pharmacies

(2) Pharmacies in hospitals and institutions

(3) Pharmacies in Government Service.

(*b*) The dissemination of this information to those responsible for the conduct of pharmaceutical service in these fields.

(*c*) To offer every facility of the AMERICAN PHARMACEUTICAL ASSOCIATION in the promotion of such service.

(*d*) To establish minimum standards for pharmaceutical practice in these three fields.

It was further moved and the motion approved unanimously, that it be recommended to the AMERICAN PHARMACEUTICAL ASSOCIATION Council that "if the AMERICAN PHARMACEUTICAL ASSOCIATION Council approves of the establishment of a Council on Pharmaceutical Practice and its objectives, that it be further recommended that this Committee be continued for the purpose of developing the plan and presenting a more perfected program to be reported to the AMERICAN PHARMACEUTICAL Council at the Portland Meeting in 1935."

The personnel of the proposed "Council on Pharmaceutical Practice" was also discussed and it was recommended that the Council should consist of the Chairman of the National Formulary Committee of Revision, the Chairman of the U. S. Pharmacopœial Committee of Revision, a representative of the American Association of Colleges of Pharmacy, a representative of the National Association of Boards of Pharmacy, a pharmacist in retail service, a hospital pharmacist and a Government pharmacist, the President of the AMERICAN PHARMACEUTICAL ASSOCIATION Ex-officio and the Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION Ex-Officio—making a total of nine members.

It was also recommended that one representative from each of the following organizations be invited to participate in the work of the Council in an advisory capacity but without a vote:

The National Association of Retail Druggists
The American Drug Manufacturer's Association
The American Medical Association
The American College of Surgeons
The American College of Physicians
The American Dental Association
American Nurses Association
The American Hospital Association
The Food and Drug Administration
The Surgeon General of the Public Health Service
The Surgeon General of the Army
(Medical Administrative Corps)
The Surgeon General of the Navy
(Hospital Corps)

All of which is respectfully submitted with the request that the proposals be promptly considered by the Council.

E. FULLERTON COOK, *Chairman.*

In this connection, the following letter has been received from President Fischelis:

To the Members of the Council:

I am glad to join Professor Cook in advocating the adoption of the suggestion to establish "A National Council on Pharmaceutical Practice" as an activity of the AMERICAN PHARMACEUTICAL ASSOCIATION. As I see the proposal, it entails a survey of existing pharmaceutical practice and the formulation of minimum standards to which pharmacies desiring the approval of the Council must adhere.

The AMERICAN PHARMACEUTICAL ASSOCIATION is already committed to a survey of pharmaceutical practice by resolutions adopted at recent conventions.

It is my belief that the establishment of "A Council on Pharmaceutical Practice" within the AMERICAN PHARMACEUTICAL ASSOCIATION organization is a forward step which will be welcomed not only by the profession of Pharmacy, but also by the medical profession and the public.

If the objectives of this Council are properly publicized, it should be possible to obtain financial support for its organization. In my judgment, this proposal should be made one of the main objectives in the campaign for funds to carry on a wider scope of activities at our Washington Headquarters.

(*Motion No. 16*) *It is moved by Eberle that the report of the Special Committee on the Proposed Council on Pharmaceutical Practice be received and that the recommendation that the Special Committee be continued for the purpose of developing the plan and presenting a more perfected program to be reported to the Council at the Portland meeting in 1935, be approved.* Comments are invited.

E. F. KELLY, *Secretary.*

LETTER NO. 10.

December 28, 1934.

To the Members of the Council:

50. Contract for Printing and Mailing the JOURNAL OF THE A. PH. A. *for 1935.* The following recommendation has been submitted by Chairman DuMez of the Committee on Publications:

> "I have carefully gone over the bids on the publication of the JOURNAL for next year, received by Dr. Eberle, and find the present publishers, namely, the Mack Printing Company, of Easton, Pa., to be the lowest bidders. This Company will also give us the best price on reprints. I, therefore, recommend to the Council that unless Editor Eberle has some good reason for making a change, the contract for publishing the JOURNAL for the ensuing year be awarded to the Mack Printing Company, of Easton, Pa."

Editor Eberle concurs in the recommendation.

For the information of the members of the Council, it is stated that the contract provides for the insertion in each issue of the JOURNAL of forms of sixteen pages, or multiples, of pharmaceutical abstracts, with separate paging and indexing, as recommended by the Special Committee on YEAR BOOK (see September 1933, issue, JOURNAL, A. PH. A., pages 914–916). It is the intention of the Editor of the YEAR BOOK to start the insertion of the abstracts for 1935 in the March issue and to issue the Report of the Progress of Pharmacy for 1934 in the usual form.

(*Motion No. 17*) *It is moved by DuMez that the contract for printing and mailing the* JOURNAL *for 1935 be awarded to the Mack Printing Company of Easton, Penna.* At the request of Chairman DuMez a vote is called for at this time but will be considered as tentative if there is objection. A voting card is enclosed.

51. Budget for 1935. Chairman Philip of the Committee on Finance submits, in accordance with Article II of Chapter II of the By-Laws of the Council, the following report on appropriations and expenditures for 1934, with a suggested budget of receipts and appropriations for 1935, which were prepared by the secretary and approved by the chairman of the Finance Committee. The officers and Finance Committee are fully aware of the difficult times we are going through, which have resulted in reduced receipts, and several items in the proposed budget have been again reduced, while others must be increased, the total being two thousand dollars more than for 1934, due largely to the increase in the appropriation for maintenance of the Building.

"To the appropriation for General Expenses in 1934 two additions were made: fifty dollars for the Section on Practical Pharmacy and Dispensing and two hundred dollars for the American Council on Pharmaceutical Education. Of the appropriations, two have been exceeded to December first. The disbursements for maintaining the Headquarters Building were $2929.92 against $1800.00 and the disbursements for the Scientific Section were $29.97 against $25.00. The latter is within the $50.00 limit for which Council action is not required In submitting the budget for 1934 it was stated that the expenses of maintaining the Building could not be estimated, and when the expenses for the year are known, a motion to increase the appropriation will be submitted. The expenses of the Committee on the Proposed Council on Pharmaceutical Practice were contributed through Chairman Cook. Charges to December 1st for General Expenses were $14,947.52 against $21,380.00 appropriated. Every effort has been made to keep the expenses below the budget appropriations.

"Under the appropriations for open accounts to December 1st, the JOURNAL charges were $7371.58 against the $11,000.00 appropriated, the N. F. $3092.98 against the $1000.00, and the Recipe Book $665.85 against the $500.00. No charges were made against the appropriation for

$50.00 for Badges and Bars. Charges to December 1st were $11,130.41 against the $12,550.00 appropriated.

"To December 1st the total budget charges were $26,077.93 against appropriations of $33,680.00 for the year, so we will not exceed our total budget.

"The receipts to December 1st show considerable variation from the estimates. From Dues, $7369.84 as compared to $7727.38 for the same period in 1933. Every effort has been made to hold this figure up, but many explain that they cannot afford the expense. Bills for dues for 1935 were mailed on December 1st and we cannot say what the total for the year will be. From the JOURNAL, $8529.85 as against $7271.15, which is very satisfactory under present conditions. From the N. F. $4712.36 for the year as against the estimate of $3500.00, which is very encouraging. From the Recipe Book, $1447.78 for the year against the estimate of $1000.00, which shows a decided gain. $2000.00 has been billed to the U. S. P. Board of Trustees for the YEAR BOOK, Volumes 20 and 21, and sales were $45.68 to December 1st.

"It has been necessary to use the income from the Life Membership Fund for the year and to transfer $1000.00 of accumulated interest to the Current Fund."

BUDGET FOR 1935.

It is very difficult to estimate receipts under present conditions. As the receipts from the sales of the National Formulary and of the Recipe Book are always approximate, the estimates for 1935 are based on the receipts for 1934. The following is suggested:

Interest	$ 100.00	
Dues	12,500.00	
Interest Life Membership Fund	5,500.00	
JOURNAL	9,500.00	
National Formulary	4,500.00	
Recipe Book	1,500.00	
YEAR BOOK	2,200.00	$35,800.00

APPROPRIATIONS FOR GENERAL EXPENSES.

No. 1	Salaries	$11,700.00
No. 2	Maintenance of Building	3,500.00
No. 3	Telegraph and Telephone	200.00
No. 4	Clerical Expenses	1,200.00
No. 5	Printing, Postage and Stationery	700.00
No. 6	Office Supplies	150.00
No. 7	Traveling Expenses	500.00
No. 8	Premium on Bonds	50.00
No. 9	Auditing	75.00
No. 10	Certificates	50.00
No. 11	Miscellaneous	200.00
No. 12	Scientific Section	25.00
No. 13	Section on Education and Legislation	25.00
No. 14	Section on Practical Pharmacy and Dispensing	25.00
No. 15	Section on Commercial Interests	25.00
No. 16	Section on Historical Pharmacy	25.00
No. 17	Commission on Proprietary Medicine	25.00
No. 18	Committee on Local Branches	25.00
No. 19	Committee on Membership	250.00
No. 20	Committee on State and National Legislation	50.00
No. 21	Committee on Syllabus	50.00
No. 22	Committee on Pharmacy Week	250.00
No. 23	Inter-Society Color Council	25.00
No. 24	International Pharmaceutical Federation	120.00

No. 25	Metric Association		10.00	
No. 26	American Conference on Hospital Service		25.00	
No. 27	American Council on Pharmaceutical Education		200.00	
No. 28	YEAR BOOK		3,500.00	
No. 29	Library		50.00	$23,030.00

APPROPRIATIONS FOR OPEN ACCOUNTS.

No. 30	JOURNAL			
	(*a*) Publication	$9,500.00		
	(*b*) Electrical Expenses	1,000.00		
	(*c*) Postage and Stationery	300.00		
	(*d*) Freight, Drayage and Miscellaneous	200.00	$11,000.00	
No. 31	National Formulary		1,000.00	
No. 32	Recipe Book		500.00	
No. 33	Badges and Bars		50.00	$12,550.00
				$35,580.00

"It will be necessary to curtail expenses wherever possible, to keep the JOURNAL within the appropriation, which will mean abstracting or condensing many papers and articles, and to advance the extra charges for the completion of the revision of the N. F. and the Recipe Book. When the Budget for 1934 was submitted, it was stated that the cost of maintaining the Headquarters Building could not be accurately estimated. The expenses for maintenance for the year have amounted to approximately $3200.00 and, with this experience, it is believed that the $3500.00 included in the budget for 1935 will be sufficient."

(*Motion No. 18*) *It is moved by Philip that the Budget for 1935 be approved as submitted.* With the approval of the Chairman of the Council, a vote is called for at this time. It will be considered as tentative if there is objection.

52. Selection of Auditors. The Chairman of the Committee on Finance recommends the employment of W. A. Johnson & Co., Baltimore, Md., to audit the accounts of the ASSOCIATION for 1934, in accordance with Article 8 of Chapter IV of the By-Laws. This Company has audited the accounts since 1922. The appropriation for the audit has been $75.00 for each year.

(*Motion No. 19*) *It is moved by Philip that W. A. Johnson & Co. be employed to audit the accounts of the* ASSOCIATION *for 1934.*

53. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 77, Thomas W. McKelvey, 3123 Union St., Bellaire, Ohio; No. 78, Yeznig P. Balouny, American University, Beirut, Syria; No. 79, Aram K. Ojakian, American University, Beirut, Syria; No. 80, Frank J. Zuck, 201 Rockford National Bank Bldg., Rockford, Ill.; No. 81, Julius Meyenberg, 114 Main St., LaGrange, Texas; No. 82, Leroy P. Baker, 1615 N. W. 27th Ave., Portland, Oregon; No. 83, Richard H. Waterman, 613 Orpington Rd., Catonsville, Md.; No. 84, James Herzog, 3168 Main St., Buffalo, N. Y.; No. 85, Augustus C. Taylor, 1733 Upshur St., Washington, D. C.; No. 86, Donald G. Sellner, 3015 Huntington Ave., Omaha, Nebr.; No. 87, John J. Goodyear, 2049 Meridian St., Indianapolis, Ind.; No. 88, Roy A. Perry, 1239 S. W. Jefferson, Portland, Oregon; No. 89, Thomas Schratz, 208 Lincoln Ave., Pittsburgh, Penna.; No. 90, William F. Siegel, 241 West Fifth St., Erie, Penna.; No. 91, Philip R. Marsh, 331 Second St., Aspinwall, Penna.; No. 92, Dale W. Yontz, Fifth St., Newell, W. Va.; No. 93, Bernard F. Stairs, 426 Main St., Mt. Pleasant, Penna.; No. 94, Rosella Lois Corsello, 3712 Brighton Rd., Pittsburgh, Penna.; No. 95, Albert J. Gabig, Jr., 319 Reamer Ave., Carnegie, Pa.; No. 96, Inez W. Henderson, 410½ N. Third St., Jeannette, Penna.; No. 97, Irene Klein, Presto, Penna.; No. 98, A R. Beamon, 157 W. 61st St., Los Angeles, Calif.; No. 99, Chieko Otsuki, 70 S. W. Salmon St., Portland, Oregon; No. 100, Victor R. Taylor, 1644 S. E. 40th Ave., Portland, Oregon; No. 101, Edward Meyer, College Station, Pullman, Wash.; No. 102, Harold C. Freed,

Route 3, Pullman, Wash.; No. 103, Mary Schoessler, 300 Campus Ave., Pullman, Wash.; No. 104, Ava Brockway, College Station, Pullman, Wash.; No. 105, Anna Merchen, 904 Campus Ave., Pullman, Wash.; No. 106, Ray C. Scholtterer, 41 Park Row, New York, N. Y.; No. 107, George D. Jenkins, 3rd and State Sts., Harrisburg, Penna.; No. 108, Pierre G. Bassett, 21 Sycamore St., New Bedford, Mass.; No. 109, W. E. Luthy, 2546 Lorain Ave., Cleveland, Ohio.

(*Motion No. 20*) *Vote on applications for membership.* E. F. KELLY, *Secretary.*

TESTIMONIAL DINNER TO R. P. FISCHELIS, PRESIDENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, HOTEL PENNSYLVANIA.

The Testimonial Dinner on January 10th, tendered to President R. P. Fischelis, by the New York Branch of the A. PH. A., was largely attended by members and visitors. The program of the function was well arranged and carried out under the direction of Chairman Hugo H. Schaefer, assisted by the Dinner Committee. The participants included members from New York and New Jersey, others came from Philadelphia, Washington and other cities.

Dr. C. W. Ballard, president of the New York Branch of the A. PH. A., presided as Toastmaster. On the dais were seated the honored guests, President and Mrs. Fischelis; Dr. and Mrs. H. V. Arny; Dr. and Mrs. C. W. Ballard; Dr. and Mrs. Charles Elliott; Charles J. McClosky; Dr. A. C. Morgan.

Toastmaster C. W. Ballard, president of the New York Branch, A. PH. A., after making introductory remarks, called on Dr. A. C. Morgan, emeritus professor of Clinical Medicine of Temple University, who reviewed the professional activities of the honored guest.

Charles H. Elliott, Commissioner on Education of the State of New Jersey, was next introduced; he spoke of the activities of the guest of honor in educational matters.

Charles J. McClosky, former president of New Jersey Pharmaceutical Association, referred to the activities of Dr. Fischelis in association and board of pharmacy matters. He was followed by former president of the A. PH. A., Dr. H. V. Arny, who spoke of associated activities and gave his address a personal touch.

The honored guest in his address discussed the activities of the AMERICAN PHARMACEUTICAL ASSOCIATION and presented his plans for greater coördination of its divisions and for larger membership.

President Fischelis was presented with a certificate of Life Membership in the AMERICAN PHARMACEUTICAL ASSOCIATION, by the New York Branch, and Mrs. Fischelis with a beautiful bouquet; New Jersey Pharmaceutical Association presented Dr. Fischelis with a gavel of an historical source.

Guests at the Testimonial Dinner, honoring Dr. R. P. Fischelis, President of the AMERICAN PHARMACEUTICAL ASSOCIATION, by New York Branch, A. PH. A., January 10, 1935.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE

The regular monthly meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Hotel Emerson, Friday, December 21, 1934. The meeting was called to order by President B. Olive Cole who introduced the speakers of the evening.

The first speaker, Wm. B. Baker, of the School of Pharmacy, University of Maryland, discussed his recent work on the standardization of aconite preparations. Mr. Baker pointed out in the course of his address that the conflicting reports of early investigators on the value of aconite as a therapeutic agent are believed due primarily to the fact that the drug and its preparations decrease rapidly in potency. The instability of the drug and its preparations is believed to be caused by the decomposition of the active principle, aconitine.

Experimental studies were made with the object in view of determining the rate of deterioration of aconite preparations, and of determining which of the stabilizers in use are the most efficient. Incidentally, the accuracy of the U. S. P. X method of assay was also studied. It was concluded that the use of hydrochloric acid as a stabilizer for tincture of aconite is superior to acetic and hypophosphorous acid as stabilizers, provided the preparations are adjusted to the correct hydrogen-ion concentration (p_H 2.3–3.0); that aconite in the form of the whole drug deteriorates rapidly and the powdered drug even more so; that the resistance of guinea pigs to aconitine is consistent, provided the weight range specified by the U. S. P. X is strictly adhered to, and further provided that these guinea pigs are in absolutely healthy, normal condition; and that the advisability of the use of aconitine as a bio-assay standard should receive more extensive consideration.

The second speaker, Wm. H. Hunt, of the School of Pharmacy, University of Maryland, discussed the bio-assay of strophanthus preparations. The therapeutic classification of the drug was given and this was followed by a discussion of the chemistry of strophanthus. It was pointed out that a considerable amount of criticism has been directed at the various bio-assay methods of strophanthus preparations. After careful investigation it was pointed out that the modified Hatcher-Brody cat method, the Trevan mortality curve frog method as modified by Chapman and Morrell, and the U. S. P. X one-hour frog method, all had been found to yield results which agreed within the limits of experimental error. Mr. Hunt further stated that the Knudson and Dresbach chemical method of assay was observed to yield inconsistent results which were rarely in agreement with the results obtained by the physiological methods.

The last speaker, Harry Rosen, also of the School of Pharmacy, University of Maryland, selected as his topic, "Pyrethrum." Among other interesting things about pyrethrum discussed by Mr. Roxen the following was especially interesting. It was pointed out that reference to another pyrethrum, *anacyclus pyrethrum*, or pellitory occurs in the literature and one should always indicate the particular pyrethrum intended. The pyrethrum known as insect flowers was

the topic of discussion. The historical and commercial aspects of pyrethrum were presented. In reviewing the chemistry of the subject it was pointed out that some volatile substance other than the pyrethrins which possess toxic activity occurs in the drug. The difference in toxicity of the drug to warm and cold blooded animals was pointed out. Finally, the various chemical and physiological methods of assay were discussed.

The papers were discussed by Drs. A. G. DuMez, R. S. Fuqua, M. R. Thompson, John Glassford, J. C. Bauer, and others present.

A rising vote of thanks was tendered to the speakers for their interesting papers.

Before adjournment, President Cole appointed the Nominating Committee for the year 1934. This committee, it was pointed out, is expected to report at the January meeting in 1935.

The committee consists of the following: *Chairman*, Aquilla Jackson; Mrs. Grace Lotz Kahler and Simon Solomon.

C. JELLEFF CARR, *Secretary*.

JANUARY.

The first meeting in 1935 of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Hotel Emerson, Friday, January 11th, President B. Olive Cole was in the chair.

The president reported on the activities of the Branch during 1934 and pointed out the general success of the organization for the year. The secretary-treasurer reported that the average attendance for the six meetings in 1934 was fifty members. The total membership now standing at 170. Particular attention was called to the new student membership in the AMERICAN PHARMACEUTICAL ASSOCIATION presented by the Branch annually to some student selected by the Faculty of the School of Pharmacy, University of Maryland.

The minutes of the December meeting were read by the secretary-treasurer and approved.

The report of the Committee on Membership was read by Chairman Gilbert Joseph. It was moved by C. Jelleff Carr that the report be accepted—carried.

The report of the Committee on Professional Relations was given by Chairman Simon Solomon, who pointed out the activities of Marvin J. Andrews in his U. S. P. and N. F. publicity work in Maryland and expressed the opinion that this was of great benefit in bringing about better professional relations between the physician and the pharmacist. In addition he mentioned the possibility of pharmacists conducting clinical laboratories or engaging in more professional types of activities. The report was discussed by Dr. A. G. DuMez who pointed out the opposition which the American Medical Association feels toward clinical laboratories conducted as accessories to retail pharmacies. He expressed his inability to understand why pharmacy students upon graduation go into purely commercial enterprises. Dr. DuMez stated that, in his opinion, the consolidation of the forces of pharmacy was necessary and that a decided effort should be put forth by pharmacists to bring about such a consolidation. Dr. John C. Krantz, Jr., stated, in discussing the problem, that the over-production of pharmacists by the schools of pharmacy was of paramount importance in producing many of our problems. It was moved by Wm. F. Reindollar that the report of the Committee be accepted—carried.

The report of the Committee on Education and Legislation was presented by Dr. A. G. DuMez. The work of the National Association of Boards of Pharmacy and American Association of Colleges of Pharmacy was mentioned. The status of the new food and drugs bill introduced into the new Congress by Senator Copeland known as S 5 was discussed. Dr. DuMez expressed the belief that some satisfactory bill would eventually be evolved whereby the old Food and Drugs act of 1906 could be amended to the satisfaction of all agencies concerned. It was moved by Wm. F. Reindollar that the report be accepted. The motion was seconded and carried.

The report of the Committee on Science and Practice of Pharmacy was presented by Chairman R. S. Fuqua; the report was comprehensive and exceedingly interesting. It was moved by Wm. F. Reindollar that the report of this committee be accepted with thanks and the committee discharged—carried.

The report of the Nominating Committee was given by Simon Solomon. After discussion the following were nominated for offices for 1935. *President*, Wm. F. Reindollar, *Vice-President*, A. N. Hewing, *Secretary-Treasurer*, C. Jelleff Carr. The secretary was instructed to cast the ballot in accordance with the wishes of the Nominating Committee.

After installation of the officers President Reindollar appointed the following committee chairmen: *Membership*, Gilbert Joseph; *Professional Relations*, Marvin J. Andrews; *Science and Practice of Pharmacy*, Dr. J. C. Krantz, Jr.; *Education and Legislation*, Dr. J. C. Bauer.

C. JELLEFF CARR.

CHICAGO.

The monthly meeting of the Chicago Branch, AMERICAN PHARMACEUTICAL ASSOCIATION, was held on Tuesday, December 18th, at the University of Illinois College of Pharmacy.

As this was the close of the year for the Branch the secretary-treasurer, L. Templeton, read a report of the financial condition of the Branch. This was followed by a report of the committee on nominations for officers for the coming year. The nominations were unanimously accepted by the members present. They are: *President*, G. L. Webster; *First Vice-President*, S. W. Morrison; *Second Vice-President*, R. A. G. Linke; *Third Vice-President*, H. M. Emig; *Secretary-Treasurer*, L. Templeton; *Delegate to the House of Delegates*, L. Templeton; *Committee Chairmen: Membership*, Thomas F. Rylands; *Legislation*, J. Riemenschneider; *Practice*, I. A. Becker; *Medical Relations*, D. Bernard Fantus; *Publicity*, A. E. Ormes.

A motion was passed to appoint a committee to draft a resolution against the repeal of the local Arvey ordinance, the repeal of which would prevent the medical schools of the city from using the impounded and unclaimed dogs for research and scientific purposes.

The speaker of the evening was O. C. Durham of the Abbott Laboratories. He discussed "Allergy from the Standpoint of the Manufacturer and Pharmacist." The following is a brief summary of the discussion.

The field of allergy is comparatively new. Only a few years back the Medical Schools were not giving training in this now important subject.

The word "allergy" was coined to mean an over-sensitiveness of the body to some particular thing. About ten per cent of the people are affected by some ordinary thing that does not affect the average person.

People only recognized the afflictions of allergism less than 100 years ago. An English doctor afflicted by pollens began an investigation. He made collections of pollens, collections of air samples, laboratory tests, skin tests and extractions; this was about 1870.

In 1903, a German doctor made serums by injecting the pollens into horses. His attention was called to the fact that the horses, by their nature of eating, probably already were inoculated with the pollens. The serums obtained were not a success.

As late as 1906 most doctors did not think that pollens caused allergisms. The idea prevailed that there was not enough pollen in the air to cause a reaction. Proof now shows that the per cent of pollen needed to give reactions is very small. The treatment now is to inject the pollen in small doses, gradually increasing the doses so that the patient becomes accustomed to the pollen. The sufferers should either take these treatments or stay away from the source of the disturbance.

Dextrose and water are most commonly used as the vehicle for pollen injection.

There are geographical, calendar and individual complications in pollen reactions. The pollens are caught on glass plates and are easily identified. This gives a clue as to what pollens are in the air and narrows down the possibilities of the ones causing the trouble. Slides were shown that gave much information as to pollen production, collection, methods of transmission and extraction.

The standard treatment is to give sixteen doses with increasing strengths. The injections are made hypodermically just below the outer skin. Skin reactions are the clue to the offending pollen. Many pollens belong to the same botanical group, hence the patient may be sensitive to all these but should be immunized only against those pollens of the group that are in the particular locality.

Mention was made of allergisms toward many things that we eat, such as rice, tomatoes and cabbage. It was emphasized that all is not known about allergism, why particular substances cause a disturbance with some people and not with others, the exact chemical nature of the substances, or how they act on the tissues of the body. However, sufficient progress has been made so that to-day extracts are made of the offending pollens and in most cases give relief to sufferers.

L. TEMPLETON, *Secretary-Treasurer.*

NEW YORK.

The December meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the Brooklyn College of Pharmacy, Long Island University, on the evening of December 10, 1934. About ninety members and their guests attended.

As the meeting was called to order, President Ballard expressed the thanks of the New York Branch to the Kings County Pharmaceutical Society for their kind invitation to hold the December meeting in the Brooklyn College of Pharmacy. The report of the secretary was then read and accepted.

Chairman Lehman, of the Committee on Education and Legislation now reported as follows:

A bill is expected to be introduced in the next Congress, instituting Unemployment Insurance, the cost of which is to be met by a 4% tax on pay-rolls. Whether the employer or the employee is to pay the tax, has not been decided as yet.

Owing to the defeat of Congressman Clyde Kelly of Pennsylvania, a valuable ally is lost to the sponsors of price stabilization: it is hoped, however, that another strong member of the House of Representatives will take up the burden of introducing another Capper-Kelly bill.

A bill amending the Pure Food and Drugs law will be offered at the next session of Congress; Senator Copeland is preparing an amended Tugwell Bill which he hopes will meet all objections. This was announced by Secretary of Agriculture Wallace on November 24th. An admirable draft of an amended pure food and drugs law was published by W. Bruce Philip, former Washington representative of the N. A. R. D., which could be adopted in its entirety, and fill all requirements.

The NRA has approved the amendment to the Retail Drug Code making the payment of assessments mandatory. The budget is still under consideration, however.

Violators of Code Laws have been found guilty by the courts in New York and Virginia. In New York the violator was guilty of substitution and the one in Virginia violated the minimum price provision.

The committee on legislation of the New York State Pharmaceutical Association intends to introduce several bills in this session of the Legislature, among them one preventing the sale of prophylactic remedies and appliances (for the purpose of preventing venereal infection) by anyone except a registered pharmacist; another, a price stabilization bill similar to the California Law (Little of Junior Capper-Kelly Bill) and also several important amendments to the pharmacy laws.

Mayor La Guardia signed the 2% sales tax law, which went into effect December 10th. Sales are taxed on all merchandise except foods, beer, physicians' prescriptions and newspapers. The tax is to be paid by the purchaser in the following manner: All sales of 12¢ or under are free of tax; all sales from 13¢ to 62¢, inclusive, 1¢ tax; all sales from 63¢ to $1.00, inclusive, 2¢ tax; 1¢ tax on every 50¢ or fraction thereof, when the amount of sale is more than $1.00.

Regarding the Bronx Drug Clerks Strike, Judge Frankenthaler denied the demand for an injunction against picketing, which was to be foreseen in the present attitude against interference with peaceful picketing. The matter will have to be argued in court.

Dr. Ballard thanked Chairman Lehman for his report and called upon Auditor Bilhuber, for a report; He announced that he had examined the accounts of the Branch and had found everything in perfect order.

Chairman Dauer, of the Committee on Progress of Pharmacy, then reported on several new proprietary preparations, among them: Tuberculin, P.P.D., Theelin in Oil, Ergone (Sensibamin), Larostidin, Gastric-Mucin and others.

President Ballard then announced the appointment of the following members on the Nominating Committee to report at the next meeting: *Chairman*, R. S. Lehman; E. A. Bilhuber and L. N. Brown.

The business part of the meeting being over, the chairman introduced the first guest speaker of the evening, Dr. Frederick Schroeder, who discussed "Modern Medicine in Relation to Prescription Writing."

Dr. Schroeder briefly reviewed some of the good work done in prescription writing propaganda last winter; he expressed the opinion that the plan of approach was, however, not entirely satisfactory, and that results were not sufficient for the time and effort spent.

In conducting the propaganda campaign the following program was followed:

1. Lecturers were sent to hospitals to discuss prescription writing with internes.
2. Formularies were mailed monthly to physicians.
3. The failure of medical schools to teach therapeutics was criticized and efforts were made to reinstate the course.
4. The exhibit of U. S. P. and N. F. products provided by Dr. Lascoff was frequently used.
5. Physicians were urged not to write for proprietary products, particularly where a similar product was official.

In all this, nevertheless, one important point was ignored, Dr. Schroeder maintained, and this was the subject he wished to discuss.

In introducing his idea, the speaker began by pointing out that therapeutics is a modern branch of medicine. The slow and late development of therapeutics was due to the fact that it is founded on a thorough knowledge of physiology, pathology and pharmacology. It has only been in recent times that great advances were made in these branches. Furthermore, the study of therapeutics was long hampered by a school of therapeutic nihilism.

In the second half of the nineteenth century real progress began with the study of the effects of drugs on animals. The profound effects of organic chemicals were soon discovered and anesthetics and disinfectants came into use. Systematic research was instituted, biochemistry became a science and provided a knowledge of vitamins and endocrines. Endocrine therapy began in 1891 with the administration of thyroid; in 1921, Insulin came into use for diabetes, and now we have a remedy for pernicious anæmia—Liver.

Progress in chemo-therapeutics and in the development of biological products is progressing rapidly, and new and far more satisfactory remedies have been found for many of the ailments to which man is heir.

The results of all of this have produced the following:

1. Preparation of medicines goes from pharmacist to manufacturer.
2. The choice of remedy becomes difficult for the physician, because of intensive advertising.
3. New standards of value are necessary in comparing these new products.

In summing up, Dr. Schroeder showed that years ago, for many diseases and ailments numerous prescriptions were written; to-day, specific biologicals are available, new chemo-therapeutic agents, or proper diet rules are followed. Systematic treatment has replaced symptomatic. All this progress in therapeutics has contributed very largely to a reduction in prescription writing. Dr. Schroeder suggested that the pharmacist keep himself thoroughly acquainted with these new advances, he should go back to an all drug pharmacy, and should direct his efforts to encouraging prescription writing among veterinarians who still use "old therapy."

Following Dr. Schroeder, the chairman introduced Dr. Jacob Sarnoff who spoke on the "Romance of Surgery."

Unfortunately it is impossible to give, in writing, a satisfactory report of Dr. Sarnoff's presentations, since most of his material consisted of special moving picture films showing surgical operations in progress. The pictures were greatly admired by every one and the comments made by Dr. Sarnoff made the presentation intensely interesting.

In connection with Dr. Schroeder's address, Dr. Sarnoff pointed out that modern surgery was also largely responsible for a reduction in prescription writing.

At the close of Dr. Sarnoff's address a rising vote of thanks was accorded both speakers.

RUDOLF O. HAUCK, *Secretary*.

NORTHERN OHIO.

The monthly meeting of the Northern Ohio Branch was held on November 9, 1934, at the Faculty Club of Western Reserve University.

This meeting was given over to discussion of the report of a committee appointed for the purpose of formulating a set of principles of coöperation between the Cleveland Academy of Medicine and the Cleveland Academy of Pharmacy.

The committee reported that in conjunction with a similar committee representing the Academy of Medicine it had adopted an expression of thought, in printed form, which will enable

both practicing physician and pharmacist to coöperate with one another for the good of the patient. This expression of thought was approved and a copy of the resolution ordered forwarded to all members on the rosters of the Academies of Medicine and Pharmacy in Cleveland. It reads as follows:

A. The welfare of the public requires a close coöperation between an intelligent well-trained medical profession and a pharmaceutical profession equally intelligent and equally well trained in its special field.

B. Personal contact between the physician and the pharmacist is essential in securing and maintaining this coöperation.

C. The relationship between these two groups is not stationery but will require a continuous modification and elaboration of concepts and principles with changing conditions.

CONCEPTS.

Following are the concepts upon which the above principles are based:

1. The public is entitled to the best possible medical care.
2. Such medical care postulates not alone competent doctors but accurate and ethical pharmaceutical service.
3. The natural corollary is that these two are mutually interdependent.
4. The mutual understanding of the codes of conduct of the two groups obviously will facilitate the service each can render to the other.
5. The establishment of an understanding acquaintance between the pharmacist and the physician who practises in his district is essential for intelligent coöperation.
6. The maintenance of this understanding once established depends upon the ability of the pharmacist to meet his obligation as a scientifically trained person.
7. This understanding acquaintance is based upon personal contact not only in the pharmacy but in the office of the physician as well.
8. Under these circumstances the discussion of mutual problems is facilitated and the obligation of the pharmacist to make available to the doctor information of the progress of pharmacy can be best met.
9. Furthermore the public is entitled to the best and most accurate professional pharmaceutical service at the lowest cost consistent with a reasonable profit to the pharmacist for this service.
10. Such a service cannot be furnished to the public through the use of proprietary medicines of known or unknown formulas since they are not designed for this purpose.
11. The use of proprietaries by doctors, either by prescriptions, sample or word of mouth, tends to favor self-medication with its attendant dangers to the patient.
12. It is the obligation of the medical men to be familiar with the action of drugs and prescription writing so that he will not have to take advantage of formulas suggested by proprietary medicine manufacturers or by their detail men.
13. The pharmacist by virtue of the accuracy of his information should supplant the detail men.
14. The discussion of details of the mechanics of pharmacy will naturally follow the establishment of this coöperation between physician and pharmacist.

By mechanics we mean counter prescribing, office dispensing, methods of handling prescribed proprietaries, cost of extra services aside from cost of materials and true pharmaceutical service and similar details affecting the working relationship between physician and pharmacist.

The ninth meeting of the Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION for the year 1934 was held at the Faculty Club of Western Reserve University, Cleveland, Friday evening, December 14th.

A resolution was passed directing the secretary to formulate certain by-laws that may be adopted later by the Branch in order that more definite standards of practice may be promulgated in relation to the public and, especially, to the medical profession. The most controversial factors involved are:

(*a*) Type of window displays.

(*b*) Relative prominence of professional and non-professional items of merchandise on counter displays.

(*c*) Itemized list of minimum equipment in the prescription department.

(*d*) Minimum list of reference books in library.

The following officers for 1935 were elected:

President, Harry E. Speer; *Vice-President*, Ellsworth Loesch; *Secretary*, Neil T. Chamberlin; *Treasurer*, Herbert Decker.

Members of the Council are:

1935, E. D. Davy, F. W. Gehrung, Eugene Remy, H. E. Speer.

1936, A. L. Flandermeyer, W. W. Hosler, Ellsworth Loesch, Edward Spease.

1937, Herbert Decker, Z. M. Gibson, N. E. Scribner, A. E. Walleck.

1938, F. J. Bacon, N. T. Chamberlin, A. P. Gegenheimer, E. L. McFetridge.

NEIL T. CHAMBERLIN, *Secretary*.

PHILADELPHIA.

The November meeting of the Philadelphia Branch of the A. PH. A. was held at the Philadelphia College of Pharmacy and Science on Tuesday evening, November 13, 1934.

The speaker was Dr. David Klein, president of the Wilson Laboratories of Chicago, who spoke on glandular products from the pharmaceutical standpoint.

He began with a discussion of the present Pharmacopœial assays for substances such as pepsin and suggested that a standard pepsin be used in connection with the present method.

For the assay of Pancreatin he suggested the preparation of a better substrate, as the starch used at present is liable to be converted in heating.

In addition to the assay for powdered Thyroid it would be advisable to include assays for the tablets and capsules as well.

He then spoke of desiccation and defatting of glandular products and mentioned the most advisable methods to be used for different glands.

The need for chemical tests for products such as anterior and posterior pituitary and liver extract was made apparent.

Dr. Klein stated that color uniformity was impossible to maintain in ovarian products because of difference in pigmentation of summer and winter foods.

He was not in favor of the use of ratios for the determination of the relationship between fresh and dried glandular materials. He suggested the adoption of standard dosages for products such as Thyroid, so as to prevent confusion among physicians.

Dr. Klein concluded his lecture with a discussion of the active principles of the ovary, pituitary, suprarenal and thyroid. Colored pictures of the glands were shown as lantern slides.

About 30 minutes of discussion preceded the adjournment.

E. H. MACLAUGHLIN, *Secretary*.

F. E. R. A. PRESCRIPTION PRICE SCHEDULE.

BY L. A. SELTZER.

Prescriptions covered by this schedule are classified as follows: Simple Liquids, Compound Liquid Mixtures, Liquids Administered in Drop Doses, Bulk Powders, Capsules, Powders, Tablets, Suppositories, Ointments, Compound Ointments, Lotions and Gargles.

Simple Liquids are those which contain one item only, such as a U. S. P. and N. F. or other liquid preparation commonly carried in readiness for dispensing. In computing the cost of *Simple Liquids*, the material is priced at 15 cents per oz., to which a fee of 25 cents is added; this sum divided by 2 constitutes the price. Thus a 4-oz. mixture should be priced at 43 cents.

Compound Liquid Mixtures are those consisting of two or more ingredients, the dispensing of which constitutes compounding. In computing the price of *Compound Liquids*, the material is priced at 25 cents per oz., to which a fee of 25 cents is added; this sum divided by 2 constitutes the price. Thus a 4-oz. mixture in this class should be priced 63 cents.

Liquids Administered in Drop Doses.—In computing the price of prescriptions of liquids administered in drop doses, the material is priced at 25 cents per oz., to which a fee of 75 cents is

added; this sum divided by 2 constitutes the price. Thus a 1-oz. or 2-oz. prescription in this class should be priced at 50 cents and 63 cents, respectively.

Bulk Powders.—In computing the price of medicine dispensed in the form of bulk powder the material is priced at 25 cents per oz. by weight, to which a compounding fee of 50 cents is added; this sum divided by 2 constitutes the price. Thus a 4-oz. prescription in this class should be priced 75 cents.

Capsules and Powders.—In computing the price of capsules and powders the material is priced at the rate of 3 cents for each unit, plus a 50-cent fee, this sum divided by 2 constitutes the price. Thus twelve units in either of those two classes should be priced 43 cents.

Tablets.—In computing the price of tablets, the price is based on the manufacturer's wholesale list plus $^1/_2$ cent for each tablet, plus a 50-cent fee; this sum divided by 2 constitutes the price.

Suppositories.—In computing the price of suppositories, the material is priced at 5 cents for each unit, plus compounding fee of $1.00 divided by 2 constitutes the price. Thus, twelve suppositories should be priced 80 cents.

Ointments.—In computing the price of ointments, the price of 1-oz., 2-oz. and 3-oz., is determined empirically at 50 cents, 75 cents and $1.00, respectively, which prices are divided by 2. In the event four or more ounces are prescribed, the material is charged at the rate of $12^1/_2$ cents per ounce plus a $1.00 fee; the sum in each case divided by 2 constitutes the price. Thus, the final price of 1-oz. should be 25 cents; 2-oz., 38 cents; 3-oz., 50 cents; 4-oz., 75 cents; 6-oz., 88 cents; 8-oz., $1.00.

Compound Ointments are those containing two or more ingredients, the dispensing of which constitutes compounding. In computing the price of *Compound Ointments*, the price of 1-oz., 2-oz., 3-oz. is determined empirically at 50 cents, 60 cents and 85 cents, respectively. In the event that four or more ounces are prescribed, the material is charged at the rate of 25 cents per oz. plus $1.00 compounding fee, the sum in each case being divided by 2. (S. L. Hilton suggests a higher basic price for ointments, because of additional time and labor required.)

Lotions.—In computing the price of lotions, the material is priced at 10 cents per oz., plus a 50-cent fee; divided by 2 equals the price. Thus, 4-oz. calamine lotion should be priced 45 cents.

Gargles.—In computing the price of gargles, the material is priced at 5 cents per oz., plus a 50-cent fee; divided by 2 equals price. Thus, 4-oz. Dobell's Solution should be priced 35 cents.

Exceptions.—In the event that in any prescription the cost of any ingredient exceeds the amount allotted as material, then the actual net cost of such expensive ingredient should be added to the amount provided for cost of material in any of the above formulas.

Specials.—Through your Committee, the F. E. R. A. has arranged to supply Insulin at 15 per cent above wholesale cost. Mineral oil, cod liver oil, milk of magnesia, etc., when prescribed in the quantities usually marketed under their respective labels and in case the labels must be replaced by a prescription label giving physician's directions for use are priced as follows: Double the ruling selling price, add 25 cents for labeling fee and divide this sum by 2.

Warning.—With reference to prescriptions dispensed which are not U. S. P. or N. F. you are cautioned that the government will not allow a larger fee than a like amount of official preparation would cost. If it exceeds that amount, you have recourse to calling the physician or returning the prescription to the patient without filling.

Do not fill prescriptions for bandages, surgical dressings or other preparations which are available for office treatments.

THE ATLANTIC CITY SESSION AMERICAN MEDICAL ASSOCIATION.

The fifteen sections of the Scientific Assembly A. M. A., have appointed exhibit committees to assist in the promotion of section exhibits at the Atlantic City session and in the coördination of activities between the Scientific Assembly and the Scientific Exhibit.

EDUCATIONAL DIRECTORY.

Part IV, Educational Associations and Directories, "Educational Directory," 1935, issued by the U. S. Department of the Interior lists the American Association of Colleges of Pharmacy and the AMERICAN PHARMACEUTICAL ASSOCIATION.

EDITORIAL NOTES

THE SOCIAL SECURITY PROGRAM.

"It is overwhelmingly important," President Roosevelt advised Congress in his special message, "to avoid any danger of permanently discrediting the sound and necessary policy of Federal legislation for economic security by attempting to apply it on too ambitious a scale before actual experience has provided guidance for the permanently safe direction of such efforts."

The *New York Times* states editorially: "Although it is truly sweeping in nature, the President's social security program has been carefully worked out with unusual precautions to keep it on a practical basis. For this reason it will be disappointing to any who expected the Committee on Economic Security to work miracles. But thoughtful students of social problems may be expected to indorse most of the underlying principles out of which this policy has evolved."

UNITED STATES CIVIL SERVICE EXAMINATIONS.

The United States Civil Service Commission has announced open competitive examinations as follows: Principal Pharmacologist, Senior Pharmacologist, Pharmacologist, Associate Pharmacologist, Assistant Pharmacologist.

Applications for the positions named for employment under the Food and Drug Administration, Department of Agriculture, must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than March 11, 1935.

The entrance salaries range from $2600.00 a year for the assistant grade to $5600.00 a year for the principal grade, subject to a deduction of not to exceed 5 per cent during the fiscal year ending June 30, 1935, as a measure of economy, and also to a deduction of $3\frac{1}{2}$ per cent toward a retirement annuity.

Certain specified education and experience are required.

Full information may be obtained from the Secretary of the United States Civil Service Board of Examiners at the post office or customhouse in any city which has a post office of the first or the second class, or from the United States Civil Service Commision, Washington, D. C.

BROADCASTS.

Purdue University School of Pharmacy, through its Extension Department, is conducting weekly broadcasts at 12:45 to 1:00 P.M. each Wednesday. The chief purpose of these talks is to impress the laity with the facts about their druggist and his position in the community in which he practices.

Such topics as "The Prescription," "The Story of Camphor," "Pharmacy in the Home," "The Clinical Thermometer," "Evolution of Drugs" and others are used. Druggists are urged to tell their customers to tune in on these talks coming from station WBAA which operates on 890 kilocycles.

PUBLIC HEALTH COUNCIL OF KANSAS.

The Public Health Council of Kansas, composed of members of the professions of medicine, dentistry and pharmacy, has been organized. The officers are: *President*, Harry Lutz, M.D., Augusta; *Vice-President*, W. C. Westacott, D.D.S., Leon; *Secretary*, MacChilds, Pharm.D., El Dorado; *Treasurer*, C. M. Kelley, D.D.S., El Dorado.

The first bulletin of the Council has been issued and gives the history of the organization, its constitution, rules and regulations. Units will be established in counties, a purpose is to supply medical and related aid and cooperate in promotions in which one or all of the professions are interested. Those desiring information anent the organization may address Secretary MacChilds, El Dorado.

A NEW BASE FOR SUPPOSITORIES.

H. Gfeller states that suppositories of cacao butter soon become rancid, and if the fat has a melting point corresponding to the lower limit of the Swiss Pharmacopœia (29° C.) they may melt in hot weather. He proposes to substitute a hardened arachis oil of m. p. 32° to 33° C. This is a lower melting point than that of the Oleum Arachidis Hydrogenatum of the new Pharmacopœia, corresponding to a lower degree of hydrogenation. The acid value of this material was 0–3, the iodine value 67.3. It becomes rancid much less quickly than cacao butter, it solidifies quickly, is odorless and colorless. The transformation of the unsaturated triolein to tristearin is an advantage as

it facilitates the incorporation of aqueous solutions.—*Quarterly Journal of Pharmacy and Pharmacology.*

PERSONAL AND NEWS ITEMS.

The Foster Hall reproductions of the songs of Stephen Foster at the central building of the Public Library were donated by Josiah K. Lilly. He devoted years to the study of Stephen Foster's work and established Foster Hall for the perpetuation of the poet's memory.

The *Merchants' Index* publishes an article on "Mankind and Medicines," by Chairman Anton Hogstad, Jr., of the National Pharmacy Week Executive Committee.

Louis Wait Rising, University of Washington School of Pharmacy, comes from Rutgers University. Prior to going to Rutgers, Professor Rising was connected with the University of South Carolina School of Pharmacy as associate professor. He received his pharmacy degrees at Oregon State College. Both Mr. and Mrs. Rising are natives of Oregon.

Dr. Wolfgang Felix von Oettingen, formerly Assistant Professor of Pharmacology at Western Reserve University, Cleveland, has been named for the supervision of the Haskell Laboratory of Industrial Toxicology of the E. I. Du Pont de Nemours Co., Wilmington, dedicated January 22nd. A complete library is to be provided for use in studying toxicological problems in the field of industrial hygiene.

Tribute is paid to **Frederick J. Wulling,** a former president of the AMERICAN PHARMACEUTICAL ASSOCIATION, under "American Contemporaries" in the News Edition of *Industrial and Engineering Chemistry,* of January 10, 1935. The writer of the article is **C. H. Rogers,** whose contact with Dean Wulling enables him to present a pen picture of a man, who is honored at home and by his associates and fellow-workers. The article was not read in time to comment on this deserved tribute.

Dr. Erwin E. Nelson, of the University of Michigan, has been appointed Principal Pharmacologist in charge of the Drug Division of the Food and Drug Administration, according to an announcement by W. G. Campbell, Chief. Doctor Nelson has already assumed his new duties.

Dr. Hugh S. Cumming, surgeon general of the United States Public Health Service, returned on December 18th after visiting Buenos Aires to attend the ninth annual Pan-American Sanitary Conference.

Eli Lilly & Co. has established under the auspices of the American Chemical Society a research award of one thousand dollars and a bronze medal to stimulate research in biological chemistry.

Sir Henry Wellcome was decorated with the Cross of the Legion of Honor of France, November 23rd.

C. H. Searle, with Mrs. Searle, is leaving within the next few days on a business trip to Honolulu, Japan, China and the Philippines.

H. J. Holthoefer has been elected for the tenth term as secretary of the Chicago Retail Druggists' Association. This is the 50th anniversary of the organization and the members are putting forth every effort to make this a successful year.

Hajime Hoshi, president of the Hoshi Pharmaceutical Co., Ltd., of Tokyo, which controls almost 20,000 drug stores in the Orient, was a recent visitor in New York.

The Winthrop Chemical Company, Inc., manufacturers of ethical pharmaceuticals, has acquired all tangible and other assets of the H. A. Metz Laboratories, Inc., with which it has been closely associated since 1926. Both companies have been engaged for many years in the development of the synthetic chemical industry in the United States.

An old-time drug store exhibit was presented to the Milwaukee Public Museum by local druggists. The suggestion for the exhibit came from John Diller who suggested it as a memorial to his brother, George A. Diller.

The Chemical Foundation, Inc., New York City, has favored the JOURNAL with a copy of "The Farm Chemurgic" by Wm. J. Hale. The author instructively presents the importance of the farm to national and industrial life. We have also received from the Chemical Foundation, Inc., a brief in the matter of a proposed reciprocal trade treaty between the United States and Switzerland submitted on behalf of Chemistry in the United States, by Francis P. Garvan, representing the Chemical Foundation, Inc., the Chemical Alliance, Inc., Synthetic Organic Chemical Manufacturers' Association, Manufacturing Chemists Association of the United States. It is a plea for chemical industry in the United States. Every business in the country, including agriculture, is becoming daily more and more dependent upon chemical industry, and the public should be informed.

The Chemical Foundation has also favored us with a reprint copy of a letter to the President from George N. Peek on foreign trade.

SOCIETIES AND COLLEGES.

NEW JERSEY FORMULARY.

The Committee on Professional Relations of the New Jersey Pharmaceutical Association and Sub-Committee on Medical Practice of the Welfare Committee of the Medical Society of New Jersey are coöperating in the development of a Formulary. A series of formulas has been endorsed and from time to time these formulas will be published and thought is being given to supplying a loose-leaf binder to physicians for filing the formulas in permanent form.

THE NATIONAL ASSOCIATION OF DRUG CLERKS, INC., TO BE DISSOLVED.

Advice has been received that it has been decided to liquidate the Druggists' National Home and dissolve the Illinois Corporation, not for profit, The National Association of Drug Clerks.

NEW JERSEY BOARD OF PHARMACY.

Failure to display a renewal certificate in New Jersey constitutes a violation of the Pharmacy Act and is punishable by a fine of not less than $25.00.

The regulations for the Act are entitled: "Pharmacy or Drug Store Defined," "Registered Pharmacist Continuously in Charge," "Permit Required," "Change of Location," "Change of Ownership," "Prescription Equipment Required," "Number of Pharmacists per Store," "Display of Permit," "Renewal of Permit," "Information Required," "Temporary Permits," "Permit Required of Each Store," "Suspension or Revocation of Permit," "Failure to Receive Notice No Excuse."

REVOCATION LAW.

"The Board of Pharmacy of the State of New Jersey may refuse an application for examination or may suspend or revoke the certificate of a registered pharmacist or a registered assistant pharmacist for any of the following causes: When the application or registration is shown to have been obtained by misrepresentation or fraudulent means, or when the applicant or registrant is guilty of chronic or persistent inebriety, or addiction to the use of narcotic drugs, or has been convicted of violating any law of this or any other State or of the United States relating to narcotic drugs, or has been convicted of violating the provisions of any law relating to the sale of liquors, or has been twice convicted of violating any law relating to the practice of pharmacy, or has been convicted of a crime involving moral turpitude, or has impersonated an applicant for registration before the Board. Before a certificate shall be refused, suspended or revoked, the accused person shall be furnished with a copy of the complaint and given a hearing before the Board. Any person to whom a certificate shall be denied by the Board or whose certificate shall be suspended or revoked by the Board shall have the right to appeal by *certiorari* to the Supreme Court for a review of such action."

HOSPITAL ABANDONS LABORATORY PRACTICE IN MEDICINE.

The custom of charging private patients in its university hospital for "purely professional services" by the laboratory departments will be abandoned by George Washington University School of Medicine, in accordance with a resolution which the faculty adopted. This action was taken in order that such purely professional fees may be handled directly between the consultant and the patient. Professional services such as the interpretation of roentgenograms and supervision of administration of roentgen therapy are the responsibility of the consultant, the resolution further points out. On the other hand, the faculty regards the technical work of its laboratories as purely nonprofessional and approves in principle the levying of charges to any person or patient for technical services rendered and for the use of its laboratory facilities. Concluding the resolution, the faculty submits the thesis that the practice of medicine in public or private laboratories, staffed by non-professional people, begins only, if at all, at the point at which such technical data are interpreted and applied to the patient for the diagnosis, treatment and prognosis of disease processes.

INSECTICIDE, DISINFECTANT ASSOCIATION.

Increased support of the code of fair competition and a closer observance of contemplated restrictive legislation pointing toward a revision in Federal and State food and drug acts were urged at the twenty-first annual meeting of the National Association of Insecticide and Disinfectant Manufacturers held December 10th and 11th.

Many scientific papers and discussions were read and interest was shown in code matters and the possibility that certain restrictive legislative tendencies would materialize. A committee was appointed to study laws, proposed laws and legislative tendencies affecting manufacturers of insecticides and disinfectants. Dr. Robert C. White asked the members for continued support. Ovid J. Roberts, NRA Deputy Administrator, who addressed the convention Tuesday, was confident that approval of the budget would be made shortly, and urged continued interest in code affairs.

The Association elected the following officers and governors: *President*, C. P. McCormick, Baltimore, Md.; *First Vice-President*, W. H. Eddy, Rochester, N. Y.; *Second Vice-President*, William Grieseiner, Baltimore, Md.; *Secretary*, John H. Wright, New York City; *Treasurer*, John Powell, New York City.

RHODE ISLAND PHARMACEUTICAL ASSOCIATION.

Rhode Island Pharmaceutical Association reëlected Clarence A. Vars, president; Joseph L. McDonald, Providence, vice-president; and James J. Gill, Providence, was reëlected secretary-treasurer. The Association, at its annual meeting in Providence on January 9th, voted to submit a list of ten names to the Governor of leading pharmacists, qualified to advise relative to pharmaceutical activities. It is understood that the purpose of the administration is to merge all activities of public health professions in one body.

BROOKLYN PHARMACEUTICAL ASSOCIATION.

The pharmaceutical associations of Brooklyn have united those bodies in one organization under the name of Brooklyn Independent Pharmacists' Association.

OKLAHOMA PHARMACEUTICAL ASSOCIATION.

Oklahoma Pharmaceutical Association is endeavoring to enact a law which will require a licensed practicing pharmacist to supervise the sale of all drugs, poisons or preparations classed as drugs. Another change provides that all moneys received over and above the expenses of the State Board of Pharmacy shall be retained by the Board as a treasury fund for the succeeding year.

Another provision strengthens the law relating to peddling of medicines and another will give to the Board of Pharmacy power to appoint its own attorney to prosecute violations of the law.

PHI DELTA CHI.

The Grand Council of Phi Delta Chi, professional fraternity of pharmacy and chemistry, will convene in annual session at the Emerson Hotel in Baltimore, February 7th–8th. Iota Chapter of the University of Maryland College of Pharmacy will be the host.

We have received from pharmacist Svend Nielsen of Copenhagen a reprint on American Pharmacy. Reference is made to the several contributions on professional pharmacy by Professor C. B. Jordan. The title of the contribution is: *Amerikanske Apoteksforhold.*

We are indebted to Secretary H. C. Christensen for a set of Proceedings, 25 volumes of the National Association of Boards of Pharmacy, from 1908 to 1933.

A serum he described as able to kill cancer cells removed from the human body and do no harm to healthy tissue similarly removed was announced December 5th by Dr. Thomas Lumsden, whose last ten years have been devoted to the fight on cancer.

A CORRECTION.

Howard H. Crosbie, writing relative to his article in November JOURNAL, page 1111, states that the second line under Fig. 1, last sentence, should read: "*Right*, After injection of 2 cc.—Sept. 12, 1934;" **not**—"*Right*, After injection of 1.75 cc.—Sept. 26, 1934." He writes that the latter statement invalidates the logic of the reading matter—we are, therefore, pleased to comply with the author's request in making the correction.

PATRICK J. CUDDYER.

Patrick J. Cuddyer, 73, S. Boston druggist, active in civic affairs, died November 30th, from a heart attack while in his drug store. His death follows by three weeks that of his wife, Mary E. Devine Cuddyer.

Mr. Cuddyer was a past-president of the Massachusetts Pharmaceutical Association and of the South Boston Citizens' Association, president of the Trade Association of South Boston, and a member of the executive boards of the Boston and National Associations of Retail Druggists.

LEGAL AND LEGISLATIVE.

REPORT OF THE COUNCIL ON PHARMACY AND CHEMISTRY ON REVISION OF THE FOOD AND DRUGS ACT IN SPECIAL REFERENCE TO DRUGS.

The following report, published in the *Journal of the American Medical Association* of January 12th, is reprinted here as a source of information on the views endorsed by the Board of Trustees of the American Medical Association on Federal food and drug legislation.

"1. To include provisions for so regulating all forms of drug advertising that it shall be truthful in statement and not deceptive by implication; the terms 'advertising' to include all ways and means of bringing articles to the attention of the public for commercial purposes.

"2. To provide that responsibility for advertising rest with the individual or firm issuing it unless such individual or firm produces a guaranty as to the truthfulness of the advertising claims, and the guarantor is amenable to the terms of the act, in which case the guarantor shall be responsible.

"3. To provide that the active ingredients and the amounts or proportions thereof in all mixed drug products not listed in official compendiums (U. S. P. and N. F.) be disclosed on the labels of such products and in the advertising of them.

"4. To prohibit the sale of drugs and drug preparations under names recognized in official compendiums (U. S. P. and N. F.), unless such drugs and drug preparations meet the standards and specifications laid down in such compendiums.

"5. To require suitable declaration on labels and in advertising of any and all habit-forming drugs, whether sold singly or in mixtures, together with explicit warning that such may be habit forming; provided that such declaration be not required in the case of drugs or mixtures of drugs dispensed on prescription, and which are to be used according to directions of a physician.

"6. To provide for official announcement by the government of such drugs as may now be held, or in the future be determined, to be habit forming.

"7. To prohibit the mention of disease names on the label of drugs or drug preparations, or in advertising thereof, unless such drug or drug preparation is a cure for the disease named; or unless such drug or drug preparation is a palliative and the nature of the palliative action is stated.

"8. To extend the provision of the law to include cosmetics and the advertising thereof, the term 'cosmetics' to include all substances and preparations intended for cleansing, altering the appearance or promoting the attractiveness of the person, unmedicated soaps excepted.

"9. To extend the scope of the term 'drug' to include devices, substances and preparations intended for the treatment of disease and all devices and all substances and preparations, other than food, intended to affect the structure or any function of the body; this provision to be for purposes of the act and not to regulate legalized practice of the healing art.

"10. To prohibit the addition of drugs to foods and confections intended or offered for general human consumption, but not to prohibit such addition to, or other modification of, foods and confections intended or offered to meet special nutritional requirements or dietary needs, provided the label and advertising of products so treated plainly declare the character and purpose of such modifications.

"11. To require that testimonials and opinions used in advertising of drugs and drug preparations be accompanied by the name and address of the writers thereof, and to consider such testimonials and opinions as advertising claims of the advertiser.

"12. To provide by permit or license or other means for government control over the sale and distribution of such drugs and therapeutic agents as cannot be adequately controlled by gross inspection or chemical examination of the finished product, except that this shall not apply to the provisions of the Serums and Vaccines Act of 1902 and amendment thereto.

"13. To require each importer, manufacturer, jobber and retailer engaged in interstate commerce in drugs and therapeutic agents to register with the government his name, place of business and the character of the business in which he is engaged or proposes to engage; such registration to be granted without cost to the applicant and accepted only on evidence showing adequacy of plant, equipment and personnel for the business proposed.

"14. To provide for coöperation between federal and state governments in the enforcement of food and drug laws in their respective

jurisdictions on a plan similar to that provided in 'An Act to Create in the Treasury Department a Bureau of Narcotics, and for Other Purposes, approved June 14, 1930.'

"15. To require labels on drugs and drug preparations to bear the name and address of the manufacturer, seller or distributor; and to bear a statement of the net weight or volume of contents.

"16. To provide for more adequate penalties, which will be commensurate with the seriousness of violations."

FOOD AND DRUG BILLS IN CONGRESS.

There are now three bills in Congress which seek to amend or displace the present Food and Drugs Act, and there is a possibility for the presentation of others.

Senator Royal S. Copeland has introduced S. 5 and this has been referred to the Committee on Commerce.

Representative James M. Mead, of Buffalo, N. Y., has presented H. R. 3972 and this has been referred to the Committee on Interstate and Foreign Commerce.

The *Druggists Circular* states that the Mead bill differs from the Copeland and McCarran bills in the senate in three major particulars: (1) It would amend the existing act, rather than write a wholly new law; (2) its definitive provisions are specific, rather than a greater or less delegation of authority to the Secretary of Agriculture; (3) it places control of advertising in the hands of the Federal Trade Commission, with injunctive relief in emergency.

Senator Pat McCarran of Nevada has introduced S. 580 which embodies the revision plan of Charles Wesley Dunn.

The numbers of the bills are given so that officers and members of legislative committees can apply to their Senators and Representatives for copies of the bills.

The president has not endorsed any of the bills, but is most interested in the enactment of a law at this session of Congress.

CAUSES FOR REMOVAL OF CODE AUTHORITIES.

An administrative order issued by the Recovery Board states causes for removal of members and employees of code authorities. These are:

(1) Conviction of code violation or removal of Blue Eagle involving any firm with which the member is in any way connected.

(2) Commission of a criminal, tortious or illegal act in connection with the activities of the code authority.

(3) Conviction of crime involving moral turpitude, after selection as a member of the code authority.

(4) Obstruction of the administration of the code.

(5) Neglect of duty.

NIRB SEEKS TO END MULTI CODE RULES.

The National Industrial Recovery Board has approved an order under which retailers will be required to pay only one code assessment regardless of the number of retail codes which affect the business. The principal line of business must be certified.

PENNSYLVANIA PRESCRIPTION TAX UPHELD.

The Supreme Court of Pennsylvania has ruled that the tax on doctors' prescriptions, provided for in the State Emergency Relief Sales Tax Act of 1932, is legal. The ruling is of importance to druggists, inasmuch as it is estimated that back taxes will have to be paid on a state tax that no longer exists.

Prescriptions in Utah come under the 2 per cent sales tax.

HEALTH INSURANCE BILL.

A resolution calling for "the best and most effective kind of federal legislation to provide a system of health insurance throughout the United States" has been introduced in the Senate by Senator Hugo L. Black of Alabama. It proposes a "full" investigation by the Senate Committee on Education and Labor.

Simultaneously, with the introduction of the resolution, the American Association for Social Security made public a social security bill which will be introduced as a model measure in 43 state legislatures.

It is understood that Senator Black later will introduce a federal subsidy bill with the social security bill as a basis, plus the findings of the Senate committee.

The bill for the states includes a health insurance system under which the great proportion of those earning less than $3000.00 a year would receive essential medical services and part compensation of loss of income by illness.

Basically, the social security measure aims at the establishment of a statewide insurance fund supported by employees, employers and

the state. The purpose of Senator Black's bill is to provide a subsidy to states enacting health insurance on the lines drawn by the social security bill.

Abraham Epstein, executive secretary of the social security organization, declared that the bill is not an attempt to reorganize medicine.—From *Drug Topics*.

ADVERTISEMENT BILL.

Representative John T. Buckbee, of Illinois, has introduced a bill under which the mails and radio would be denied to a person disseminating misleading advertising, penalty is provided.

TAX-FREE ALCOHOL.

Representative Woodruff of Michigan introduced H R 1425 which would authorize the withdrawal of alcohol tax-free for the use of any clinic operating for charity and not for profit, including use in compounding of bona fide medicines for treatment outside of such clinics but not for sale.

BOARD DIRECTED TO ISSUE LICENSE.

In a Mississippi case a pharmacist who had been granted a license in Louisiana applied for a license in Mississippi. The law makes it mandatory that the State board of pharmacy license as a registered pharmacist any person of good moral character who had after examination been licensed to practice pharmacy in another state prior to December 31, 1927. A review of the case states that the Board had taken no action in the matter and hence the court action. After review of the case the court reversed the judgment of the lower court and directed the State Board of Pharmacy to issue a license to the applicant to practice as a registered pharmacist.

DRUG STORE SIGNS IDENTIFY THE ESTABLISHMENT.

The defense in four cases in California were found guilty in each case and appealed: their appeals were consolidated. Two cases were reversed because the complaint failed to prove and there was no proof adduced to show that the signs designated in the law were displayed on the store owned by the defendants. The court accordingly reversed the convictions in these two cases. In the other two, because of an error in assessing penalties on these defendants, the cases were remanded to the trial court with directions to impose the proper penalties.

WEST VIRGINIA CHAIN STORE LICENSE TAX UPHELD.

The right of states to levy a tax on chain stores was upheld by the Supreme Court of the United States in a recent decision of a case brought by the Standard Oil Company of New Jersey.

The decision specifically upheld the chain store license tax which is in force in West Virginia.

RECOMMENDATION FOR REVISION OF NRA.

The National Industrial Recovery Board has received a memorandum from the Consumers' Advisory Board containing recommendations for the revision of the National Industrial Recovery Act. Although there has been no opportunity for formal consideration of these recommendations, which were submitted January 5th, the National Industrial Recovery Board immediately made them public in the belief that discussion of all such proposals is desirable.

BLUE EAGLES.

The National Industrial Recovery Board announced recently that Blue Eagles for particular trades and industries marked "1934," as well as those originally issued under the President's Reëmployment Agreement, may be used in 1935.

NARCOTIC PEDLERS SENTENCED.

Fifteen narcotic pedlers were sentenced by Judge William H. Atwell in the United States District Court at Dallas.

TAX COMMISSION REFUNDS IN OHIO.

The Tax Commission of Ohio has issued a notice to dealers relative to refunds on unused cosmetic stamps. The Cosmetic law was repealed January 1st and there will be no cosmetic tax until after the sales tax receipts are obtainable by dealers.

A MISLABELED ELIXIR OF TERPIN HYDRATE AND CODEINE.

A qualifying word, such as "special," used in conjunction with the name of a product listed in the National Formulary, is not sufficient legal grounds for varying an N. F. formula, Judge D. J. Patterson of the United States District Court, Southern District of

New York, ruled in the case of the United States of America against seized bottles of Elixir Terpin Hydrate and Codeine.

Testimony showed that the product did not conform to the standard required by the National Formulary. The claimant contended that the word "special" after the name on the label was an indication that the product is not the Elixir of Terpin Hydrate and Codeine defined in the Formulary, but is a variation. After hearing testimony Judge Patterson gave the following opinion:

"The question is not what the chemist or the druggist may understand by the addition of the word 'special' to the title. The Food and Drugs Act was passed as a protection to the uninformed, that they might be assured that an article purchased was what it purported to be.

"Certainly the average consumer would not be put on guard that a compound called 'elixir terpin hydrate and codeine (special)' was not the elixir of terpin hydrate and codeine listed in the formulary. The word 'special' might well signify to him merely that the ingredients were especially pure or that the product was manufactured with special care. If a manufacturer wishes to use a National Formulary name for a non-conforming product, it is his duty to give the public unmistakable notice that in its composition there has been a departure from the formula given in the Formulary."

The Judge then quoted from the regulations for enforcement of the Food and Drugs Act, Regulation 7 (b), which provides: "A drug sold under a name, or a synonym, recognized in the United States Pharmacopœia or the National Formulary which does not conform to the standard of strength, quality or purity for the article as determined by the test laid down therein shall be labeled with a statement to the effect that the drug is not a United States Pharmacopœia or National Formulary article."

On the basis of this, Judge Patterson ruled that the bottles were misbranded.

Judge Patterson also gave his opinion on whether there was adulteration or misbranding on the score that the contents of the bottles did not correspond with the declarations on the labels. His opinion on this read, in part:

"The labels stated that each ounce contained one grain of codeine sulphate and eight grains of terpin hydrate. There was testimony by government chemists that on analyses there was more terpin hydrate than the quantity declared and less codeine sulphate. On the other hand, there was testimony that when compounded the products had precisely the quantities specified on the label, and there was testimony that the test for terpin hydrate is not a satisfactory one.

"The variations found by the government chemists, taken as a whole, are not wide, and I am not prepared to say that they are beyond the zone of experimental error and tolerance in manufacture. The burden of proof is on the United States, and the proof does not establish adulteration or misbranding by reason of discrepancy between the quantities set forth on the labels and the contents of the bottles.

"There will be a decree of forfeiture for adulteration and misbranding. Findings in conformity with this opinion may be submitted."—*Drug Trade News.*

TAX ON TOILETRIES.

It is stated that the battle in Congress will be to prevent an increase in taxes on toiletries and not in an effort to eliminate the taxes.

NEW NRA POLICY OF PUBLICIZING DRUG-CODE VIOLATIONS.

Settlement of a complaint against Ford's Cut Rate Drug Stores, Buffalo, N. Y., which charged violation of the loss limitation provision of the retail drug code has been announced by the NRA Compliance Division. The settlement, which was in the form of an affidavit signed by Otis C. Altfeld, is the first to be announced by the Compliance Division under a new policy which contemplates full publicity concerning alleged code violations.

Complaint was filed by S. N. Vaughn, secretary of the Buffalo Retail Drug Code Authority. A number of specific violations were charged in an affidavit presented to the board by Mr. Vaughn, among them being the selling of many products at cut prices.

The National Industrial Recovery Board has appointed Dr. Gustav Peck as assistant to the Administrative Officer on employment problems in codes and their administration. This appointment is in line with the Board's policy of allotting specific problems to personnel well versed in the subjects assigned them.

Dr. Peck was graduated from Columbia University and received his Ph.D. degree from Brookings Institution.

OBITUARY.

FREDERICK BARNETT KILMER.

Frederick Barnett Kilmer, director of the laboratories of Johnson & Johnson, New Brunswick, N. J., and father of Joyce Kilmer, the poet who was killed in action in France, died December 28th, at his home in New Brunswick, aged eighty-three years.

Mr. Kilmer was born in Chapinville, Conn., the son of Charles Kilmer, a Methodist clergyman, and Mary Ann Langdon Kilmer. He was educated in the public schools of Binghamton, N. Y., Wyoming Seminary, Kingston, Pa., and the New York College of Pharmacy. He took special courses in chemistry at Columbia, Yale and Rutgers. He owned a drug store in New Brunswick before he was chosen to head Johnson & Johnson's scientific department in 1899.

Mr. Kilmer had been president of the New Brunswick Board of Health, adviser to the New Jersey State Board of Health and a member of the American Public Health Association. He was a member of a number of foreign and American organizations, among them, the American Chemical Society, the American Institute of Chemical Engineers, the Chemists Club of New York. He was a former vice-president of the American Drug Manufacturers' Association, and a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1886.

Mr. Kilmer married Miss Annie E. Kilburn, December 25, 1871. They had four children, all of whom are dead. Mrs. Kilmer died three years ago. Further reference is made to the deceased on page 3 of this issue of the JOURNAL.

JOSEPH H. DOW.

Joseph Henry Dow, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, well and favorably known Maine pharmacist, died at his residence in Portland, December 29th, aged 76 years. He was chairman of the Entertainment Committee when the ASSOCIATION met in Portland.

Mr. Dow was born in Portland, the son of Joseph and Sara Dow, and attended the Portland public schools. He was a charter member of the Portland Cadets, rising in rank to sergeant and 2nd lieutenant, but withdrawing upon his acceptance of a position as a drug salesman with Cook, Everett and Pennell which entailed long absences from Portland. He was one of the original members of the Cadet drill squad, and in recognition of his interests in this organization and his services to it he was elected every year from 1910 president of the Cadets, and in 1928, life president of the Honorary Association.

As a salesman for two Portland firms and with Brewer and Co. of Worcester, his connection at the time of his death, he traveled all over the State for 55 years and had friends in every community that boasted a drug store.

Partly as a result of this wide acquaintance, Mr. Dow conceived the idea of forming the Maine Pharmaceutical Association. He was for many years a member of its executive committee, and for 15 years had been chairman of its committee on general arrangements for the annual meetings.

He was also instrumental in the formation of the Maine Commercial Travelers' Association, in which he from time to time held office.

Surviving him are his son, Walter P. Dow; two daughters, Mrs. Guy F. Dunton and Mrs. Vertner A. Stahl; and two brothers, George W. of West Southport, and Charles, now a resident of California. His wife, who was Annie C. Curtis of Biddeford, died in 1909.

SMITH C. WILSON.

SMITH C. WILSON, member of the AMERICAN PHARMACEUTICAL ASSOCIATION and prominent in Nebraska drug circles, died December 8th, at Bryan Memorial Hospital, Lincoln, aged 73 years. The following is prepared from a sketch by Secretary J. G. McBride.

Born at Bergens Mills, New Jersey, Mr. Wilson came west half a century ago and since that time had been in the drug business. He first went to Cheyenne, Wyoming, and later moved to St. Louis, where he joined Meyer Brothers' wholesale drug house. Mr. Wilson then became connected with the Capital Drug Company, a Lincoln wholesale concern, and later entered the retail business.

In 1929, he was elected president of the Nebraska Pharmaceutical Association in which he had worked for forty years. Through his association work he was one of the best known and most influential druggists in the state.

Last February, Mr. Wilson was elected president of the Nebraska Society of the Sons of the American Revolution. He was one of the two Nebraska members of the Society of Cincinnati, deriving his eligibility from the

New Jersey branch. His descent was through his mother from Captain James Anderson.

The following letter from John O'Brien, of Omaha, is reprinted from the *Northwestern Druggist:*

"Smith was a man gifted with rare ability. He was vigorous, hopeful and uplifting. He was endowed with great capacity for work, illuminated with a great purpose, unrivalled in aggressiveness, rich in sympathy and consideration for his fellowmen. His genius has often been shown in the constructive work that he did in local, state and national pharmaceutical affairs for the past thirty years. He has served in the ranks. He has served as chairman of every committee in his state organization, and he has filled the office of president with honor to himself and credit to his fellowmen. Smith Wilson was a man of his convictions and he had the moral courage to pass them on to others, not by dictation but by arguments addressed to common sense.

"Mr. Wilson's hobby was organization work and he took a great interest in attending conventions and delighted in renewing old friendships. He boasted that he had only missed one meeting of the N. Ph. A. in forty-five years. Almost yearly he attended the conventions of the Iowa, South Dakota, Kansas and Missouri associations. He was a lover of the out-of-doors and never missed a chance to fish or hunt. Only this fall he made a trip of over one thousand miles to hunt pheasants in Dakota.

"He is survived by one son and a grandson, his wife having preceded him in death five years ago."

HUGO KANTROWITZ.

Hugo Kantrowitz, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1907, died January 18th, at his home in Richmond Hill, N. Y., aged 80 years.

The deceased was born in Breslau, Germany, April 8, 1854, and came to this country with his widowed mother and other members of the family in 1856. He received his early education in Philadelphia and as a youth was employed with the *Philadelphia Demokrat*, a German newspaper. In 1878, he removed to New York and engaged with the *New Yorker Zeitung*.

In 1880, the *Deutsche Apotheker Zeitung* was established and in its promotion and service Mr. Kantrowitz was active until its discontinuance a few years ago, and as editor and publisher he furthered a relation of German and American pharmacists which reflects credit. The *Zeitung* was the official organ of the German Apothecaries Society and maintained a professional relationship with other pharmaceutical publications and the editor was always a welcome visitor in their offices. He took a deep interest in the Veteran Druggists' Associations and the German Apothecaries Society and was an honored life-long member of both organizations.

He was a member of New York College of Pharmacy, Columbia University, of New York Pharmaceutical Association, of the German Press Club (New York) and of the Steuben Society of America. He was a regular attendant at the annual meetings of the State association and of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Mr. and Mrs. Kantrowitz celebrated their golden wedding anniversary in 1926; the latter and a daughter, Mrs. Claire Muller, survive the deceased. Nathaniel Nicolai in speaking of him said: "At an age well past seventy—he enjoyed life more like a youth just experiencing his first freedom. More than fifty years he served pharmacy—loyally, unselfishly, gladly, efficiently. He served both continents—was known in Europe as well as in the United States, the country of his adoption; was universally respected and beloved. The German apothecaries, here, owe much to his life and work."

ISRAEL H. SHURTLEFF.

Israel Hammond Shurtleff, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1875, died in New Bedford, Mass., on December 15th, while engaged in his pharmacy, a business founded by him in 1878.

Mr. Shurtleff was born in Mattapoisett, Mass., April 7, 1849, the son of Alvah and Joana Shurtleff. After the completion of his earlier education he engaged with James E. Blake and, later, with William A. Pease of New Bedford. In 1878, he entered business on his own account and continued actively until his death; his son, Frederick A. Shurtleff, is now the manager of the pharmacy. Mr. and Mrs. Shurtleff celebrated the golden anniversary of their marriage in 1880.

Mr. Shurtleff had been a member of the Massachusetts State Pharmaceutical Association since its organization and a member of the Independent Order of Odd Fellows for more than fifty years.

BOOK NOTICES AND REVIEWS.

Our Willie. By JOHN URI LLOYD, author of Etidorpha, Stringtown on the Pike, Red Head, Warwick of the Knobs, Scroggins, Felix Moses the Beloved Jew. Published by John G. Kidd & Son, Inc., Cincinnati. 375 pages. Price $2.50.

In reviewing a book by one who has contributed largely to the success of the AMERICAN PHARMACEUTICAL ASSOCIATION, has served well in its offices and held membership in it for a longer period of time than any other member and is still deeply and actively interested, the reviewer very willingly permits the promptings of friendship and regard to accompany his thoughts, even though they do not enter into these lines. Preceding books by the same author were read by this writer as issued and copies of them are part of his library—this personal note will be pardoned.

This year the author of *Our Willie* celebrated his 85th birthday and the story is published more than thirty years after a large part of it had been written; it was completed because of a promise to Mrs. Lloyd a few days before her departure on November 27, 1932.

Our Willie may be designated a companion volume to "Stringtown on the Pike," in it the author introduces Silas and Sarah, of the primitive highlanders of Boone County, Kentucky. The love for their son who has brought hope and happiness to their humble home also becomes the source of grief. The characters depicted play their part before the readers—"pathos, humor and thrilling action form a trinity that endows the plots and counterplots of the book with the vividness of reality, spiced with a mystery that intrigues the reader's interest."

Clara is the heroine, the childhood sweetheart of *Our Willie* is constantly loyal, "Judge Elford is the lovable but just judge, who impresses the readers with the majesty as well as the humanity of the law; Squire Gettem is the villain, who is the nemesis of *Our Willie*, of Silas and Sarah, of the slave boy Kola and who almost outwits Judge Elford."

Daily life of the section, night echoing with muffled hoof beats and war days add to the action of the story.

The illustrations are interesting, they are from photographs by Mrs. J. U. Lloyd, Olita Lloyd, daughter of J. T. Lloyd, and the author is the youthful fisherman in the frontispiece. J. K. Lilly has contributed a reproduction of the front cover of Stephen A. Foster's Melody, "Willie We Have Missed You," dated 1854.

Hand Book of Chemistry. Compiled and edited by NORBERT ADOLPH LANGE, Ph.D., Assistant Professor of Organic Chemistry at Case School of Applied Science; Lecturer in Organic Chemistry at Cleveland College of Western Reserve University; member of the American Chemical Society and of the Deutsche Chemische Gesellschaft—assisted by Gordon M. Forker and Richard Stevens Burington, Ph.D., Assistant Professor of Mathematics at Case School of Applied Science; published by Hand Book Publishers, Inc., Sandusky, Ohio. 1545 pages. Price $6.00. Bound in fabricoid.

This Hand Book of Chemistry differs from other books of this kind because of the large amount of material contained for those engaged in all divisions of the chemical industry. The author states that this book is the result of a number of years' experience in compiling and editing of data useful to chemists. An effort has been made to select material to meet the needs of chemists who should have the information at hand or without prolonged search, and for those who have not the facilities of a large technical library.

In glancing through the pages one is impressed with the successful effort made to select a great variety of information from all branches of science as well as in the commercial fields. The information presented is in condensed form, much of it arranged in a tabular way so as to conserve space and give the information that is needed by chemists, physicists, mineralogists, engineers, librarians, patent attorneys, pharmacists, dieticians, manufacturers, physicians and others. Thus are tabulated physical constants of inorganic compounds, nomenclature of organic compounds; names and formulas of organic radicals are given together with information regarding name, synonym, formula, boiling and melting points, etc. Other tabulations are concerned with properties of materials as to their physical, thermal properties, etc.

Among outstanding new features is information regarding hazardous chemicals, their handling; changes in atomic weight, between 1894 and 1933; a mineral table, tables for water chemists, classification of crystals, organic reagents, laboratory solutions, etc.

Other pages are given over to refrigeration, antifreeze solutions, definitions of pharmaceutical terms and various conversion factors.

A number of pages list and define laboratory solutions. A number of pages are given to laboratory arts and recipes. More than 200 pages are devoted to logarithms in varied calculations and applications.

The extent of information given is represented by the index of thirty pages.

Modern Drug Encyclopedia and Therapeutic Guide. by JACOB GUTMAN, M.D., Phar.D., F.A.C.P. Consultant, Manhattan General Hospital, New York; Riverside, Shore Road, Williamsburg Maternity and Borough Park General Hospitals, Brooklyn; formerly Professor of Materia Medica, College of Dentistry, University of State of New Jersey; Professor, Clinical Chemistry, Jersey City College of Pharmacy; Instructor in Medicine, New York Post-Graduate Medical School and Hospital; Attending Physician, Wyckoff Heights and Unity Hospitals, Brooklyn. Publisher, Paul B. Hoeber, Inc., 76 Fifth Ave., New York. 1394 pages. Price $7.50.

The author states that this treatise is designed to meet the demand of the progressive physician for information concerning the most modern therapeutic agencies placed at his command by research laboratories. It presents without bias or comment all the popular non-pharmacopœial preparations and other remedies found useful in the treatment of disease.

The contents is presented in 15 chapters, including the following: 1040 Drugs of Known Constitution and Action, 408 Effective Combinations of Two or More Fully Defined Ingredients, 346 Preparations of Unstated or Incompletely Defined Components, 860 Endocrine Preparations, 1563 Hypodermic Medicaments, 535 Biologicals, 2223 Individual and 121 Group Allergens, 209 Foods and Beverages, 122 Bottled Mineral Waters, Natural and Artificial, 644 Miscellaneous Products, Therapeutic Guide, Bibliography, Manufacturers and Distributors' Index, Drug Index.

The titles of the divisions indicate the purpose and scope of the book, for which there is evidently a need and the extent of the references is presented by an index of 220 pages. The encyclopedia deals largely with medicinals that are controlled by manufacturing houses and gives the name of each house in connection with that of the medicinal; one section of the book is given over to an alphabetical list of the names and addresses of the manufacturers, under each of which names is a list of the house's specialties.

Most of the information contained in the volume may be found in medical and pharmaceutical publications and literature sent out by manufacturers, but reference thereto is not readily located unless indexed, hence, physicians, pharmacists, dentists and nurses will find "The Encyclopedia and Therapeutic Guide" a valuable time-saver.

WAGNER BILL, S. 1130

The Committee on Economic Security in a report states that it is not prepared *at this time* to make recommendation for a system of health insurance. Coöperation has been asked of advisory groups representing the medical and dental professions and hospital management in the development of a plan for health insurance which will be beneficial alike to the public and the professions concerned.

Senator Wagner of New York has submitted S. 1130, known as the Wagner Bill for Social Insurance, which provides for a social insurance board appointed by the President. The Committee on Economic Security recognizes that the successful operation of a plan depends in a large measure upon the provision of sound relations between the insured population and the professional practitioners or institutions furnishing medical services under the insurance plan.

The report of the Committee submits the main lines along which its studies are proceeding: The fundamental goals of health insurance, the administration of the services of the medical professions, exclusion of commercial or other intermediary agents, the basis of benefits of the insurance, the payments for the service, state-wide basis under a federal law, cash payments in partial replacements of wage loss, cost of health and medical services, correlation of existing health and medical services, health and medical services for persons without income.

The Committee concludes that—"The rôle of the federal government is conceived to be principally (*a*) to establish minimum standards for health insurance practice and (*b*) to provide subsidies, grants or other financial aids or incentives to states which undertake the development of health insurance systems which meet the federal standards.

As the measure will affect pharmacy, it is necessary for pharmacists to study its trend, so that they may coöperate in shaping this important legislation.

NOTICE TO CONTRIBUTORS TO THE JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION.

The following notice has been prepared from comments received from members of the Board of Review of Papers and of the Publication Committee.

Manuscripts should be sent to Editor E. G. Eberle, 2215 Constitution Ave., N. W., Washington, D. C.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled. The original (*not* carbon) copy should be sent. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense for a limited number of figures and plates will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

References to the literature cited should be grouped at the end of the manuscript under the *References*. The citations should be numbered consecutively in the order of their appearance (their location in the text should be indicated by full-sized figures included in parentheses). The sequence followed in the citations should be: Author's name (with initials), name of publication, volume number, page number and the date in parenthesis. Abbreviations for journals should conform to the style of *Chemical Abstracts*, published by the American Chemical Society.

(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

Papers presented at the Sections of the AMERICAN PHARMACEUTICAL ASSOCIATION'S annual meeting become the property of the Association and may at the discretion of the Editor be published in the JOURNAL. Papers presented at these Sections may be published in other periodicals only after the release of the papers by the Board of Review of Papers of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The Editor will appreciate comments from Board of Review and Committee on Publication, members, authors and others interested.